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VOL. 23, NO. 4

APRIL 2002

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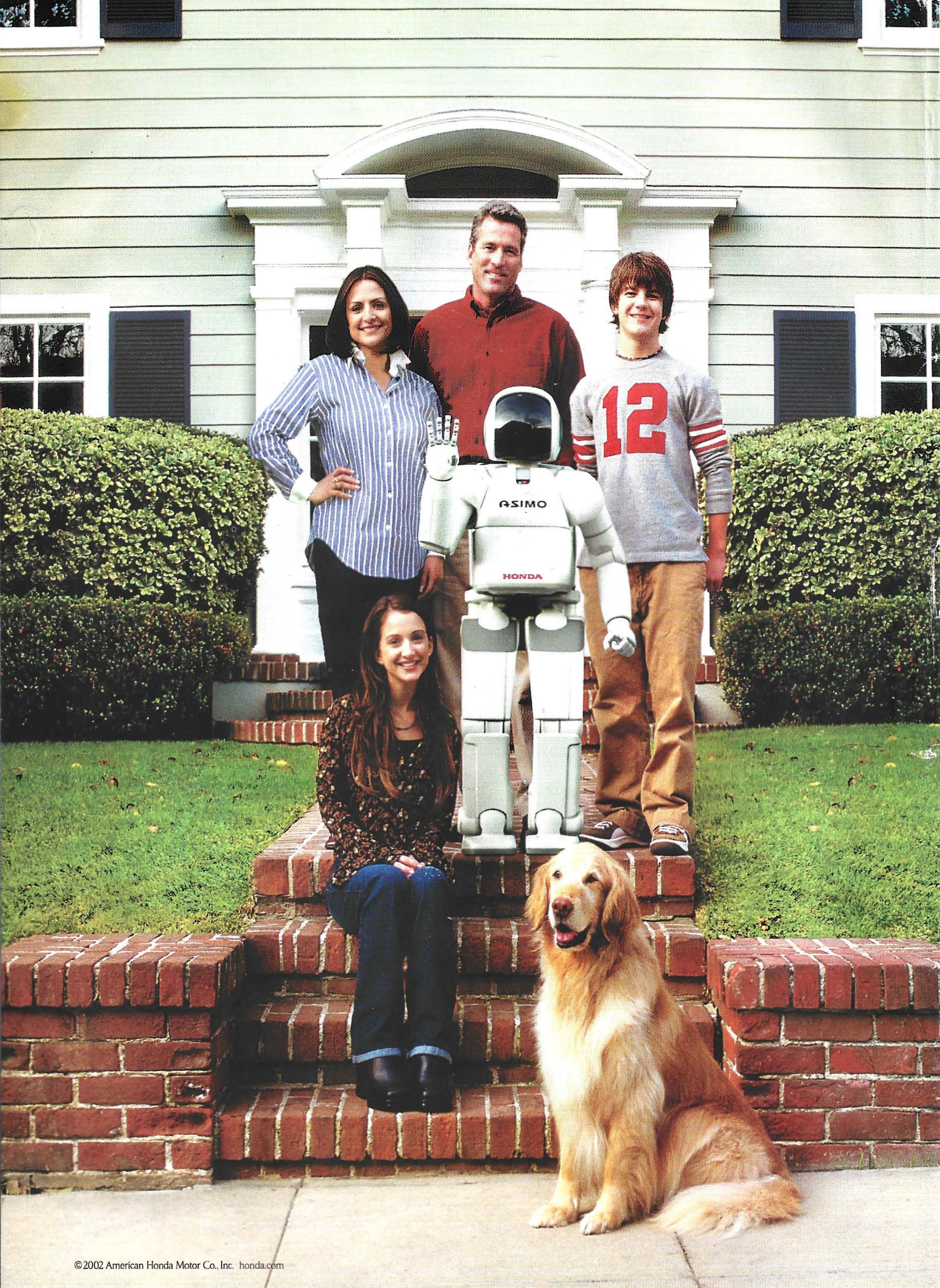
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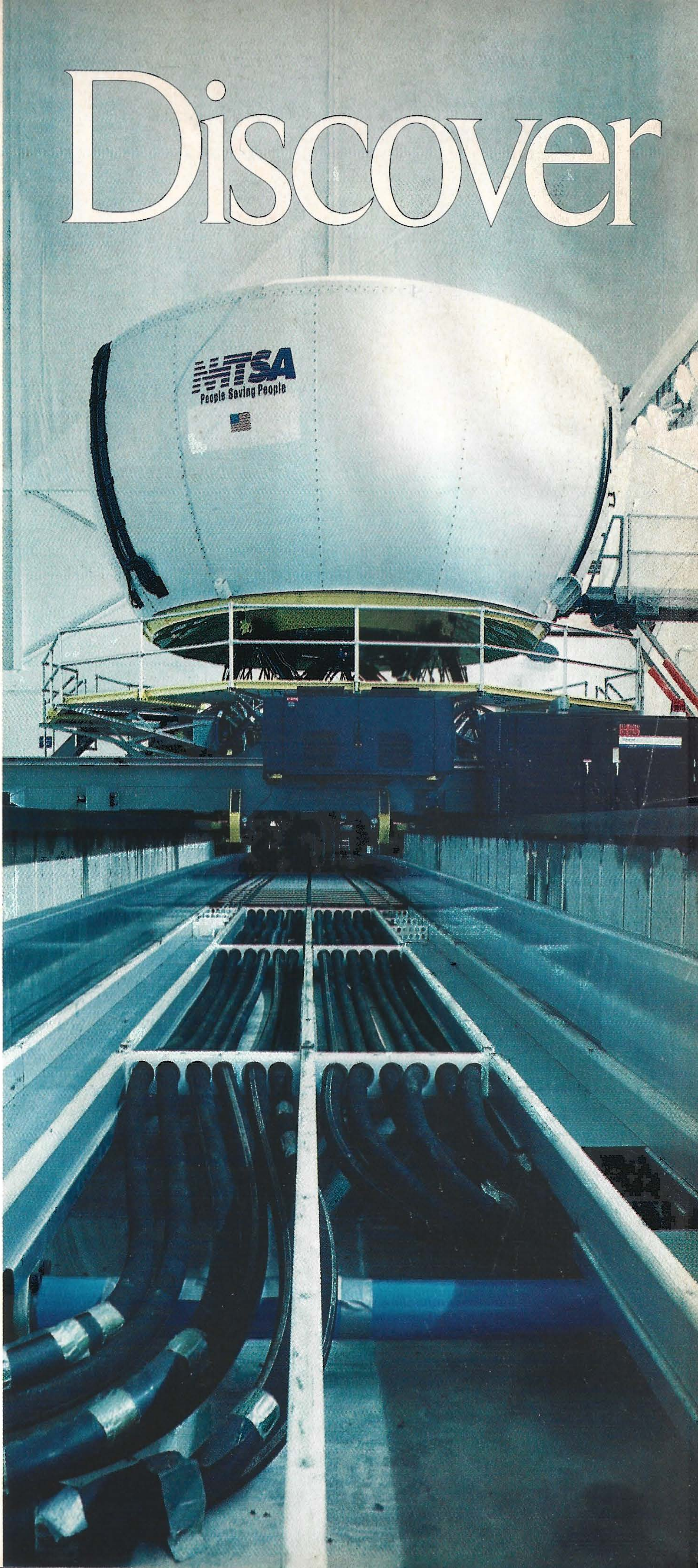

RIGHT: WITHIN THIS DOME SITS THE COCKPIT OF THE WORLD'S BEST DRIVING SIMULATOR, WHERE THE DROWSY, WOOZY, DRUNK, AND INQUISITIVE STEER A COURSE FOR SCIENCE. SEE PAGE 40.
ON THE COVER: PHYSICIST ALAN GUTH CONTENDS THAT WE LIVE IN A "FREE-LUNCH UNIVERSE"—A NO-STRINGS GIFT THAT POPPED OUT OF NOWHERE. PHOTOGRAPH BY MICHAEL GRIMM. SEE PAGE 32.

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PHOTOGRAPH BY KATHARINA BOSSE

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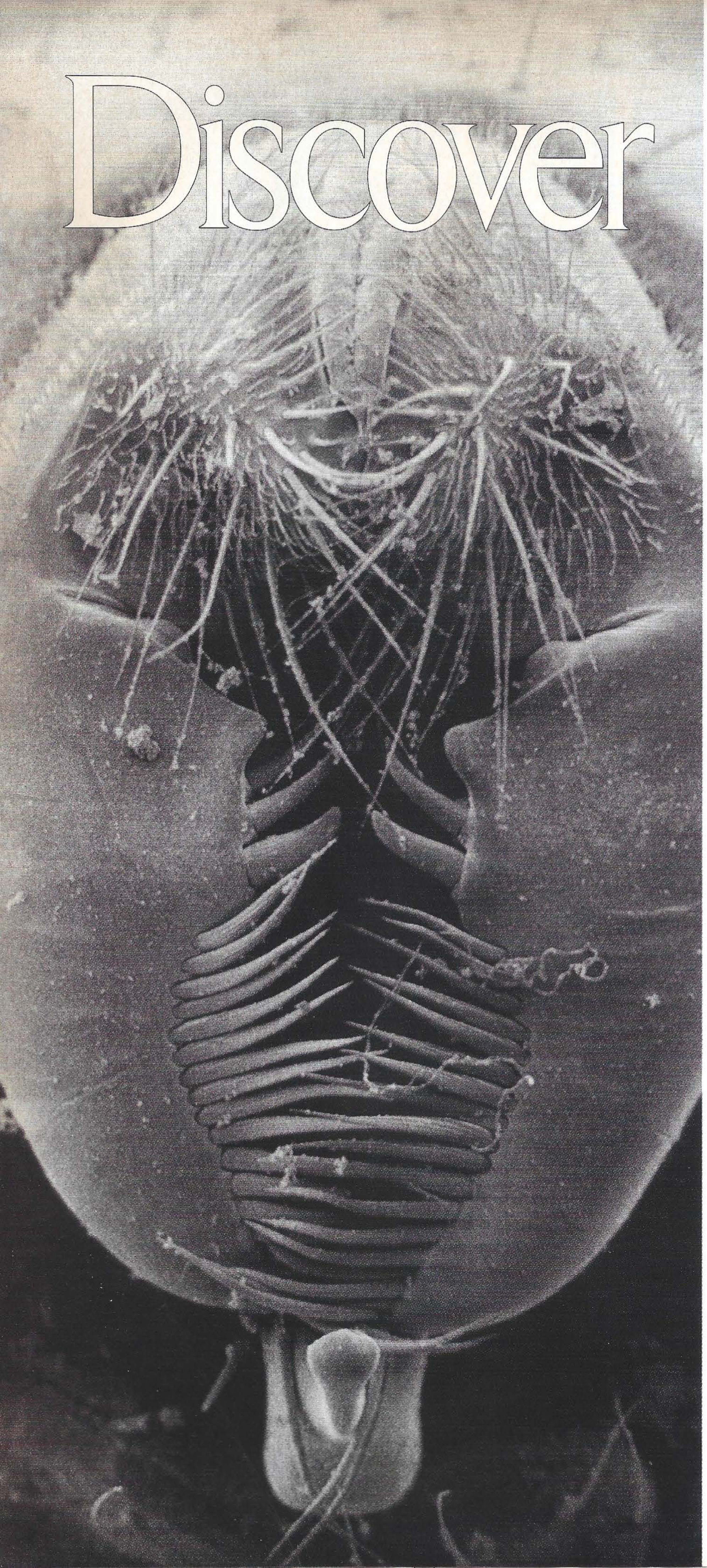

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PHOTOGRAPH BY DAVID GRIMALDI.

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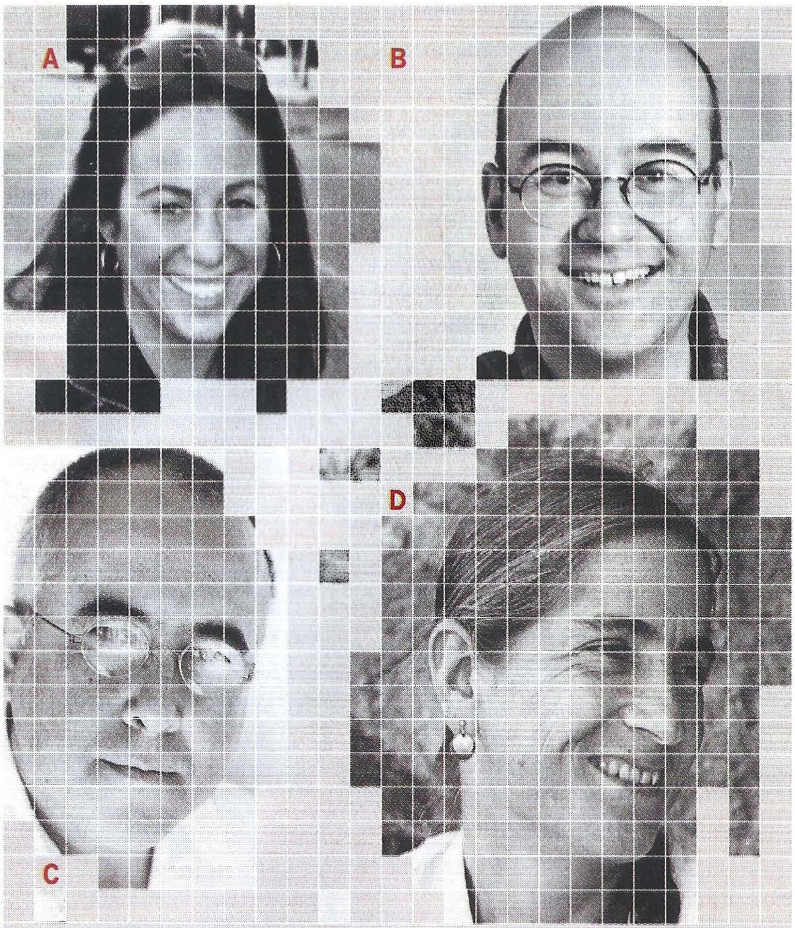

GILLIAN LAUB (A) When photographing pioneering gene therapists Brad Margus and David Cox at Perlegen Sciences in California ("Bad Genes, Good Drugs," page 52), "I decided to take honest, simple, straightforward portraits," says Laub, who shoots frequently for *Newsweek* and *The New York Times Magazine.* "They are men on a mission, but despite everything they've done, they're still very direct and easygoing—just normal guys doing more than the normal things."

SAM HOOPER SAMUELS (B) His father was a chemical engineer. His mother trained as a chemical engineer and taught physics and chemistry. His brother became a biochemist. So when Samuels persisted in pursuing a career as an actor, his family was, he says, "very polite but sure it was a pipe dream." Once he became a science journalist ("Driving Simulator," page 40) and turned his attention to subjects they loved, his family members seemed "incredibly relieved."

MAX AGUILERA-HELLWEG (C) Twelve years ago, after this photographer ("Do We Kill Whales With Sound?" page 60) was assigned to shoot spinal surgery, he decided to apply to medical school. "I'd never seen the inside of a body before—it felt like going to the moon," he recalls. "I became obsessed with recapturing that sense of awe, which is part of what led me to become a doctor." Aguilera-Hellweg is in his second year at Tulane's School of Medicine in New Orleans.

SHARMAN APT RUSSELL (D) "I enjoy writing about science because it's like getting little sequential M.A.'s," says Russell ("Talking Plants," page 46), who first got a master's degree in conservation biology. While she loves her work, she sometimes looks over her shoulder and wonders: "A part of me envies the fieldwork of scientists. The serenity of botany is my version of the religious impulse."

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1926
1927
LITTLE AMERICA
1929
1933
3
U.S. POSTAGE
3
CENTS

This stamp was produced in 1933.

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RIDDLE ME THIS

In "The 11 Greatest Unanswered Questions of Physics" [February], Eric Haseltine left out one question: What caused the Big Bang? I think the answer is unknowable and outside the realm of science. I remember a Russian scientist saying about 30 years ago that the Big Bang could have been caused by the high-speed collision of two particles, neutrons for example. So is the answer truly unknowable? Does it make any sense to speculate on the cause of the most important event in the history of the universe? If so, why was it not on the list of the 11 most important questions?

TOM HAMMER—Hockessin, Delaware

Eric Haseltine responds: *There are many ideas about what caused the Big Bang. One provocative theory postulates that the universe is eternal and simply goes through oscillations that periodically produce big bangs. Imagine that in the distant future, gravity wins out over the forces currently driving the universe apart, collapsing the universe into a dense state that gets so hot it explodes in another big bang, only to eventually run out of steam, collapse, and repeat the cycle ad infinitum. Although the rate of expansion of the universe is increasing, there is no theoretical reason why this expansion couldn't slow in the future, as many inflation theories argue it has slowed in the past. Another theory is that the universe simply popped out of the vacuum in the same way that virtual particle-antiparticle pairs emerge from empty space, only to recombine and vanish with a burst of energy. In this scenario there would be an "anti-universe" somewhere out there with which we may ultimately reconnect. A lot of scientists are uncomfortable speculating about the causes of the Big Bang because no one has come up with a way to test these theories. Any hypothesis that cannot be tested and proved false falls more into the realm of philosophy than physics.*

I read Eric Haseltine's article with much interest. However, I was disappointed that there were only 11 questions. It seems the National Research Council is looking at the trees (particles) and not the forest (purpose). A unified theory of the universe must include the most important theory of all—the nature of life itself. Could some of the unknown forces, particles, and energies described in the article be responsible for life? Or does life spring up spontaneously, fueled by some energy or particle yet undiscovered? Who cares if we understand all the physics behind the universe if we can't answer the question of how life starts?

MARK MITTEREDER—via the Internet

I have some questions to be added to your list of the greatest unanswered questions of physics. As I sit here typing this, I ask myself, "Can modern physics explain the space-time motion of the atoms and electrons that make up my computer? Can they explain why they just happen to be here today? Can physics explain the travels of the metal atoms that make up the wires and those peculiar arrangements of silicon in the glass and on the chips?" If the ultimate goal of physics is to be able to explain the space-time motion of everything *at all scales,* then it seems most inadequate at explaining the space-time motion of objects on the human scale. Physics is very good at describing the space-time movements of the very large, like super-galaxies, and the very small, like quarks and atoms, but at the scale where I work and breathe, in my day-to-day interactions with my fellow man and woman, physics does not explain much about the space-time movements of the objects swirling about me.

JEFFREY ROSEMAN, M.D., PH.D., M.P.H.
Birmingham, Alabama

"The 11 Greatest Unanswered Questions" was very enlightening to me, a geological engineer with a passion for astronomical history. I have a problem, however, with the answer to where the heavy elements came from in conjunction with the dark-matter quandary. Earth and other rocky planets are rich in heavy elements. These planets are huge accretions of matter and sometimes have massive iron concentrations. The article indicates that these elements traveled across space from supernova events. Could the dark matter that is being sought be heavy elements or the precursors of heavy elements? Since supernova events still appear to occur, why isn't space still full of heavy elements? If supernovas in fact don't still occur, why isn't space chock-full of unaccreted heavy elements, like a fog?

MIKE WHIMS—Wixom, Michigan

(continued on page 86)

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NEWS ABOUT SCIENCE, MEDICINE, AND TECHNOLOGY

SILICON GOES POW! Normally tame substances can pack a wallop when chopped into bits. "Gunpowder blows up because the finely divided carbon in it oxidizes so fast that it burns," says Michael Sailor, a chemist at the University of California at San Diego. Now he has figured out how to do the same trick with silicon (left), creating computer chips that blow up on command. The chips are made from silicon crystals coated with gadolinium nitrate, a more stable oxidant than the potassium nitrate used in gunpowder. "It won't blow up until you apply a slight charge. We did it with a 9-volt battery," Sailor says. The exploding chips might be useful in portable chemical detectors. Tiny, controlled detonations could heat and vaporize a sample, causing it to emit radiation that would reveal its precise composition. Speck-size devices could then sniff for explosives or for biological weapons. Detonating silicon could also provide the ultimate computer security in sensitive applications—"like the triggers for nuclear weapons, which you want to be able to disable completely if they get into the wrong hands," Sailor says. What about *Mission: Impossible*-style cell phones and laptops? "People like the idea of a stolen cell phone that will self-destruct in five seconds, but there are lots of better ways to disable the chip inside your phone," Sailor says. *—Kathy A. Svitil*

Rogue Genes South of the Border

WHILE PREPARING A WORKSHOP ON DNA DETECTION IN OAXACA, MEXICO, David Quist found a surprise: an alien gene embedded in a sample of native corn, known as criollo. The alien was actually familiar, a type of gene commonly found in the genetically modified crops grown in the United States. Indeed, Quist observed the same DNA signature in a can of American corn he had brought for comparison. But this was an ancient strain of maize cultivated in the remote mountains of southern Mexico. How did the gene get there?

Quist and Ignacio Chapela, both microbial ecologists at the University of California at Berkeley, performed a comprehensive study of criollo in the region. Sampling four fields more than 12 miles from the closest mountain road, the researchers discovered that the native corn had incorporated not one but several genes found in engineered American corn. One sample of criollo even contained the gene for Bt toxin, an insecticide derived from bacteria.

How these genes migrated into Mexican criollo remains a mystery. Pollen grains can carry genes from engineered plants into nearby native strains or even into closely related weeds, but in 1998 Mexico banned the planting of genetically modified crops. Chapela suspects farmers may be planting imported corn originally distributed as food, or that migrant workers may be bringing samples back from the United States. Whatever its source, the genetic pollution could have grave consequences. Corn originated in this region, and it is here that it is most genetically diverse. "If you lose that diversity, you lose the possibility of finding disease-resistance genes in the future," says Chapela. "It's a serious challenge to food security worldwide." *—Josie Glausiusz*

Greenpeace activists in Mexico protest genetically modified corn. Since 1998, the Mexican government has banned the planting of such crops but still allows the importing of modified grain from abroad. American farmers now plant millions of acres of genetically modified corn and other crops.

PHOTOGRAPHS: TOP, COURTESY OF FREDERIC MIKULEC/UCSD; BOTTOM, AP PHOTO/BRAVO.

I'm awake, you're asleep: The reason may be rooted in a mix of environment and innate genetic programming.

Night Owls vs. Early Birds

SOME PEOPLE HIT THE GYM RUNNING IN THE MORNING while others groggily slam the snooze button. Neuroscientist Jeanne Duffy of Boston's Brigham and Women's Hospital believes much of the difference is rooted in biology—specifically, in the innate sleep-wake cycle known as the circadian rhythm.

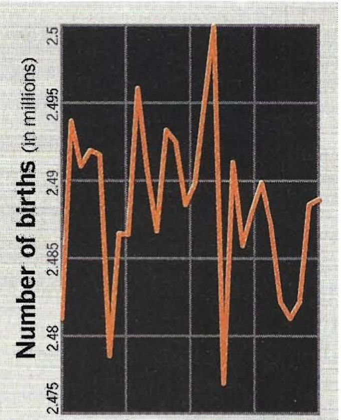
Duffy and her colleagues studied sleep patterns among 17 men who lived in a controlled laboratory setting for one month. On average the period of the circadian rhythm is around 24 hours, but it varies from person to person. The researchers isolated the subjects from all cues that could indicate the time of day in order to bring out the natural circadian rhythm. Duffy then noticed an eye-opening pattern: The circadian periods of self-described "morning people" are consistently shorter than those of the "night people." These results bolster an earlier study, in which the same team found that evening types awake at or shortly after their peak hour of sleepiness, a stage in the circadian cycle marked by grogginess, low body temperature, and high levels of the hormone melatonin in the bloodstream. Morning types, in contrast, tend to wake well past the peak sleepiness phase, even though they get up earlier in the day.

"This explains why morning types are perkier and feel more alert when they first get up. Evening types are waking right when their alertness is at its absolute worst," Duffy says. These and other findings may elucidate why people's sleep patterns become generally more morninglike as they age, causing them to tire early. She also hopes her work will illuminate the mechanism behind delayed sleep phase syndrome, which causes mild insomnia that can lead to learning problems among many high-school students. —*Maia Weinstock*

PHOTOGRAPHS: CLOCKWISE FROM TOP, ERIC WEEKS; COURTESY OF CSIRO EXPLORATION AND MINING.

By the Numbers

DON'T BLAME IT ON THE MOON Folk wisdom holds that more babies are born during the full moon than at other times. Many doctors and nurses agree. Astronomer Daniel Caton of Appalachian State University wondered if anyone had ever put the claim to a test. After unearthing a few inconclusive studies, he began to hunt around for a data set large enough to yield reliable statistics. He and his students collected data on 70 million births over the past 20 years from the National Center for Health Statistics. Then they painstakingly entered the numbers into a computer to search for patterns. At last, Caton can deliver an unambiguous verdict: The phase of the moon has no influence on the number of babies born. "The full moon is the most obvious moon—it rises at sunset and it's up all night. People remember what they happen to notice," Caton says. Next, he hopes to tackle another bit of lunar folklore, which claims that more crimes and emergency-room admissions occur when the moon is full. —*Solana Pyne*

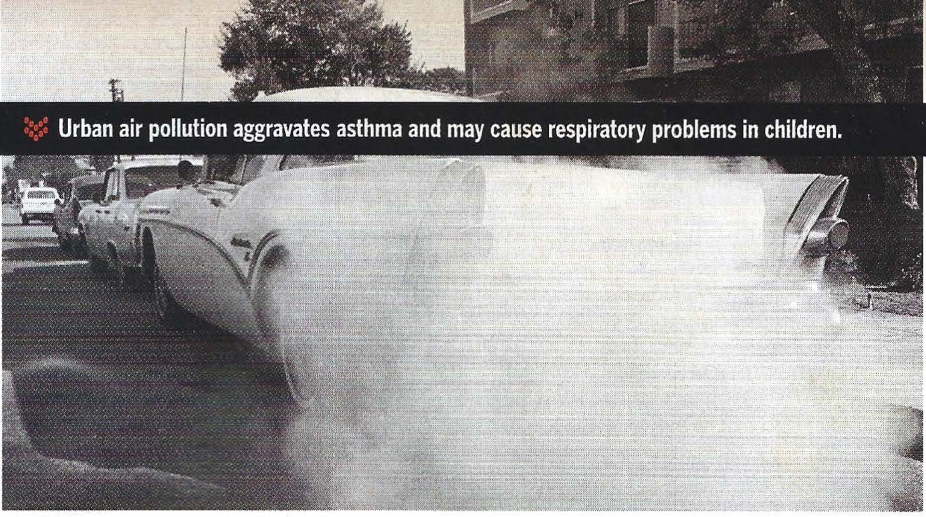


> 'The most wonderful mystery of life may well be the means by which it created so much diversity from so little physical matter'
>
> —*E. O. Wilson*

EARLY BREATH OF FRESH AIR

SCIENTISTS HAVE LONG BELIEVED THAT Earth's atmosphere contained little free oxygen until 2.3 billion years ago, when the first photosynthetic bacteria evolved. Neil Phillips, a geologist at the Commonwealth Scientific and Industrial Research Organization in Australia, began to doubt the conventional wisdom while studying gold deposits in South Africa. He uncovered what appear to be pisoliths, pellets of iron oxide (above) thought to arise only in the presence of oxygen. But these pisoliths date from 2.8 billion years ago, long before the rise of oxygen-spewing microbes.

Phillips argues that Earth probably had an oxygen atmosphere from the beginning of geologic history. If so, ideas about how life evolved during the first 2 billion years could be wrong. But some of his colleagues propose that the pisoliths could have formed under anoxic conditions, pointing to geologic and experimental evidence against early oxygen. "To my mind, this issue has been solved for 30 years," says James Kasting, a geoscientist at Pennsylvania State University. —*Lauren Gravitz*



Urban air pollution aggravates asthma and may cause respiratory problems in children.

FETUSES TAKE AIR POLLUTION TO HEART

PREGNANT WOMEN EXPOSED TO TWO COMMON pollutants may give birth to babies with heart deformities, says epidemiologist Beate Ritz of the University of California at Los Angeles. She collected daily air pollution measurements from 30 locations around L.A. and correlated them to local birth registries. For women in areas with the highest levels of carbon monoxide and ozone, the risk of having a child with certain heart malformations and valve defects was triple that of women living in the least noxious neighborhoods. In moderately polluted areas, the risk was double. "The dose-response relationship is just about the closest you can get to a smoking gun in this kind of study," says Ritz.

Normally, two children in a thousand are born with such heart defects, which can be life threatening and require corrective surgery before age 1. In the most polluted areas, the incidence jumped to six per thousand. "The effects are probably much greater even than we're detecting because the worst cases result in miscarriages," Ritz says. She can't yet say which pollutants are to blame, as carbon monoxide levels may just be a marker for other harmful particles or chemicals, but the intensity of the effect shocked her: "Carbon monoxide is principally an indicator of car exhaust, and nearly every urban center in the country has exhaust levels that would be dangerous to pregnant women." *—Jocelyn Selim*

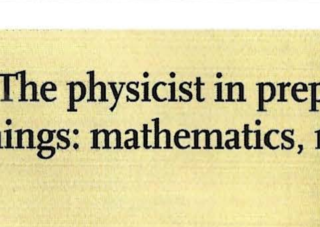
> **'The physicist in preparing for his work needs three things: mathematics, mathematics, and mathematics'**
>
> ***—Wilhelm Conrad Röntgen***

Ask the Wizard

Why do our ears ring? ***DIMETRA POWELL, BALTIMORE, MARYLAND***

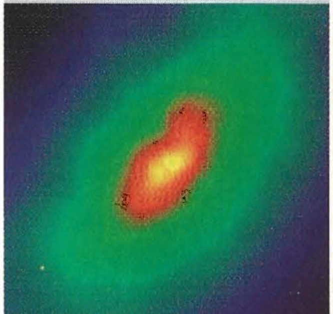
Robert Folmer of Oregon Health and Science University's Hearing Research Center replies:

Ringing in the ears is a form of tinnitus, the perception of sound that does not have an external source. Tinnitus can be constant or intermittent and can include buzzing, hissing, or sizzling. Many people experience momentary tinnitus, a high-pitched tone that lasts five to 30 seconds. This transient sensation probably results from changes in blood flow or cellular activity within the inner ear. Acute tinnitus, which can last days or weeks, may be caused by infection, medication, head injury, accumulated earwax, or changes in blood pressure or chemistry. Tinnitus is most commonly caused by exposure to loud sounds such as music at a rock concert, power tools, or gunfire. The subsequent ringing indicates damage to the stereocilia, tiny hairlike structures attached to cells in the inner ear. Moderate sounds cause stereocilia to make small movements, triggering the release of neurotransmitters in the ear that activate auditory nerves in the brain. Excessive noise bends the stereocilia out of shape. People then commonly hear a high-pitched ringing because the hair cells that respond to higher-frequency sounds are most easily harmed by loud noises. If the damage is modest, stereocilia generally return to normal and the ringing stops. Repeated exposure to hazardous sounds eventually destroys hair cells, resulting in permanent hearing loss and long-term tinnitus.



LET THERE BE LIGHT

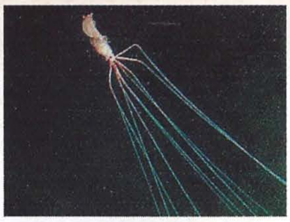
ASTRONOMERS ARE CLOSING IN ON ONE OF the most enigmatic periods of cosmic history—the era when stars first lit up the darkness of space. A recent analysis of a Hubble Space Telescope image hinted that massive stars were born en masse in a giant conflagration a few hundred million years after the Big Bang. Observations from the 2MASS ground-based map of the infrared sky confirm the early fireworks. Alexander Kashlinsky, an astrophysicist at NASA's Goddard Space Flight Center in Greenbelt, Maryland, and his colleagues processed 2MASS data to filter out nearby stars and galaxies. The remaining glow, produced by galaxies that formed when the universe was less than a billion years old, was two to three times brighter than expected. "It means galaxies were forming stars at a gigantic rate," he says, more than 30 times faster than in our galaxy today.



A model of the first stars forming.

Astrophysicist Michael Norman of the University of California at San Diego and his colleagues created a supercomputer simulation to peer even deeper in time. Their model indicates stars started forming 100 million years after the Big Bang, much earlier than previous estimates. Those pioneer stars, 100 times more massive than our sun, condensed from hydrogen and helium gas, "pristine stuff from the Big Bang," Norman says. Such huge stars would have lived a few million years before exploding as supernovas. But during that brief time, they synthesized the first heavy elements—the carbon, nitrogen, calcium, and other materials that eventually found their way into planets and life. Until now, cosmologists had little information about when and how the earliest stars formed. "We're shedding light on an epoch that hadn't received much attention. So for now, we're the dogma," Norman says. *—Kathy A. Svitil*

PHOTOGRAPHS: CLOCKWISE FROM TOP, BETTMANN/CORBIS; COURTESY OF UCSD; LYNN GOLDSMITH/CORBIS.



20,000 LEAGUES UNDER In the inky depths of the ocean, scientists have spied a translucent squid with oversize fins and angel-hair tentacles long enough to hug an SUV. First spotted off Brazil in 1988, the deep-sea curiosity was seen seven more times over the next 13 years before anyone could get a good look. Then cephalopod biologist Michael Vecchione of the National Marine Fisheries Service in Washington, D.C., saw the squid up close in video footage taken by a submersible in the Gulf of Mexico. The stringy creature, as yet unnamed, reaches 23 feet in length. Vecchione suspects it is the adult version of a peculiar squid he and his colleagues had previously identified from three juvenile specimens. These creatures may look freakish, but they could be ubiquitous more than a mile below the surface, where all the sightings have occurred. Scientists still know little about the ecosystem at those depths. "This is just one example of a large animal that is completely unknown. There's a huge volume of space that needs to be explored," Vecchione says. —*Solana Pyne*

Science Surfing

Find Your Way Around the Genome (gslc.genetics.utah.edu)
Read about genetic functions or try hands-on educational activities at this friendly site.

Dig Up History (archnet.asu.edu)
A library of links to archaeological information, research news, and museums around the world.

Explore the Strangest Theory in Physics (www.superstringtheory.com)
Clever explanations and diagrams explain the strange idea that particles act like plucked strings.

The Four-Minute Race Eraser

ROBERT KURZBAN THINKS EVOlution offers hints to combat racism. Kurzban, an evolutionary psychologist at the University of California at Los Angeles, speculates that the primal impulse to spot allies prompted people to use race as a clue about allegiance. If other visual clues were better indicators, he says, people would pay less attention to race. He and his colleagues tested the idea by having volunteers watch videos showing conversations among groups of two African American men and two white men. Next, sentences were displayed alongside photos of the people who said them. At the end of the study, the volunteers were asked to match sentences with the speakers.

Volunteers initially mixed up the speakers mostly along racial lines. But in a second video, the speakers wore colored T-shirts that divided them into two teams. This time, volunteers confused statements between members of the same team more often than between members of the same race, evidently paying less attention now to skin color. It took just four minutes to erase racial categories, Kurzban says. —*Solana Pyne*

Who belongs to which group? When other factors take precedence, people stop categorizing by race.

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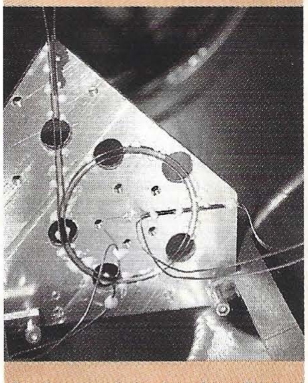
ATOMIC MERRY-GO-ROUND

AT A TIME WHEN COLLEAGUES ARE building larger, ever-faster circular atom smashers, Michael Chapman's work looks like a parody. He and his fellow physicists at Georgia Tech have built a particle-storage ring less than an inch wide; the cold atoms inside travel at just two miles per hour. But this toylike device has a serious goal: It may allow scientists to control atoms the way lasers control light.

Chapman's team calls their ring the Nevatron, a play on the mile-wide Tevatron particle accelerator at Fermilab outside Chicago. The Nevatron (shown below) consists of two closely spaced circular wires attached to an aluminum plate. Electric current creates a magnetic field that confines atoms between the wires. The researchers cool rubidium atoms until they barely move and inject them in. "Then they just loop around like a carnival ride," Chapman says.



He envisions using the Nevatron as a sensitive gyroscope for aircraft guidance systems. Two streams of cold atoms running in opposite directions around the ring would interfere with each other, a process that is highly sensitive to motion. A properly tuned device could therefore pick up every change in the flight path of an airplane. Ultimately, Chapman hopes to cool the atoms further so they emerge from the Nevatron as a Bose-Einstein condensate, a state of matter in which atoms blend together into a quantum blur. Under those conditions, atoms form a coherent beam, like the photons of light in a laser. An atom laser could serve as a superaccurate clock or as a tool for exploring the enigmas of the quantum world, where atoms can cancel each other out or exist in two places at the same time. —*Fenella Saunders*

PHOTOGRAPHS: CLOCKWISE FROM TOP, COURTESY OF TEXAS A & M UNIVERSITY; COURTESY OF GEORGIA INSTITUTE OF TECHNOLOGY; GRID CLOCKWISE FROM TOP LEFT: AP PHOTO/BURHAN OZBILICI; AP PHOTO/KEVORK DJANSEZIAN; AP PHOTO/ARKANSAS DEPARTMENT OF CORRECTIONS; AP PHOTO/TENNESSEE DEPARTMENT OF CORRECTIONS; AP PHOTO/MAX NASH; AP PHOTO/ERIC DRAPER.

LANDMARKS

April 10 30th anniversary of the signing of the Biological Weapons Convention, a treaty banning bio-warfare, by the United States and the U.S.S.R. The U.S. recently opposed creating an inspection regime to enforce the treaty.

April 15 550th anniversary of the birth of Renaissance man Leonardo da Vinci.

April 23 135th anniversary of the patenting of the zoetrope, an early device to show moving pictures, by William Lincoln. Figures on its inside wall appear to move when viewed through a slit in a spinning cylinder.

TRIBUTES

Won Maureen Raymo of Boston University received the $10,000 Cody Award in Ocean Sciences from the Scripps Institution of Oceanography in San Diego. An expert on the origin of the ice ages, Raymo has proposed that the weathering of mountains has cooled Earth over the past 40 million years by drawing carbon dioxide from the air.

Died Graham Ryder, 52, on January 5. A lunar geologist, Ryder cataloged the cache of rocks carried back by the Apollo missions. His research helped unravel the history of the moon's crust.

Died Aleksandr Prokhorov, 85, on January 8. The Russian physicist co-developed the maser, a variant on the laser that emits microwave radiation of a single wavelength. He received a Nobel Prize in 1964 for this work.

Carbon nanotube transistors with gold contacts—the tiny future of computers?

Computers Enter the Molecular Zone

IN 1974 TWO RESEARCHERS, MARK RATNER OF Northwestern University and Ari Aviram of IBM, had a wild vision. They imagined a day when computers would use individual molecules to perform digital calculations, yielding machines of breathtaking capability. That day is near: Two groups of researchers have just developed the first practical logic circuits whose components have been shrunk to the size of molecules.

No matter how they're constructed, computer circuits work by guiding electricity through a sequence of on-off amplifiers, or transistors. Charles Lieber, a chemist at Harvard, downsized the transistor, using silicon or gallium nitride wires just 10 atoms thick. He and his collaborators created a grooved template that forms little tunnels when placed on a flat surface. Then they forced a liquid containing the silicon wires to run through those tunnels. "Like logs in a river, the wires line up in the flow," Lieber says. Finally, the researchers rotated the template and repeated the process with gallium nitride wires, creating a crosshatch pattern in which each intersection functions as a transistor. The completed circuits have successfully performed simple addition problems.

Cees Dekker of Delft University of Technology in the Netherlands and his colleagues had previously built similarly small transistors from cylindrical carbon molecules, called carbon nanotubes. Now they've spread thousands of nanotubes on a chip, three of which they attached to aluminum contacts and joined together with gold bridges to create a simple test circuit. It may take a decade or two before either approach leads to a practical molecular computer, but Dekker now can imagine how it will happen: "We have single molecules combined to make a logic circuit. That was the holy grail with this field for 25 years." *—Fenella Saunders*

Old Disease in the New World

EUROPEANS BROUGHT PLAGUE AND PESTILENCE TO THE Americas—but maybe not as much of it as historians say. After taking X rays of more than 200 mummies in Peru, imaging specialist Jerry Conlogue of Quinnipiac University found that 10 percent of the bodies showed bone abnormalities characteristic of tuberculosis. That means TB, long considered a disease imported from Europe, was present in the New World 1,000 years ago. Conlogue admits his analysis isn't 100 percent accurate. "But the spines show the signature erosion patterns. It's classic TB." In modern populations there are four instances of moderate TB for every one in which the disease advances enough to affect the bones. If the same statistics held among the pre-Incan peoples of the Andes, over half the population was suffering from the disease—enough to contribute significantly to the culture's decline. Conlogue thinks the moist climate fostered transmission of the disease. His studies suggest the Spanish conquistadors faced a population weakened by a tough lifestyle. "Nearly a quarter of the mummies showed signs of osteoarthritis brought on by heavy labor, there are signs of severe malnutrition, and severe periodontal disease was rampant," he says. *—Jocelyn Selim*

X rays of mummies from precolonial Peru indicate TB preceded the Europeans.

PHOTOGRAPHS: CLOCKWISE FROM TOP, COURTESY OF TU DELFT/GRIPP; COURTESY OF GERALD CONLOGUE/QUINNIPIAC UNIVERSITY; TIMEPIX.

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DISCOVER DIALOGUE: ECONOMIST JEFFREY SACHS

GOOD HEALTH, GOOD WEALTH

PHOTOGRAPH BY EMILY SHUR

Jeffrey Sachs spent much of the last decade advising countries from Bolivia to Mongolia on how to overhaul their economies. Now the Harvard economist has a new mission: to overhaul the world's health. As chairman of the World Health Organization's Commission on Macroeconomics and Health, he recently oversaw a report showing that a modest investment in health care in poor countries—$34 a person a year—would not only reduce disease but would be a boon for the global economy. He discussed this linkage with associate editor Josie Glausiusz.

What led to your interest in the economics of human health?

I was spending time in very poor countries, and I was shocked by the amount of dying I was seeing. I was working in Zambia in the mid-1990s on a project with the Central Bank. Roughly seven or eight of my 30 professional counterparts on that project died of AIDS within three or four years. I started to ask whether this disease burden was impacting economic performance.

How does poor health hinder economic performance?

Take malaria. In most cases people with malaria are sick for a few days and stay home from work. But you also have losses of tourism and foreign investment, you have limitations on international trade, you have reductions of migration into and out of malarial regions. Or you go out to the villages in Malawi, where a whole generation is being lost to AIDS. There are a few grandmothers there and dozens and dozens of orphaned children. If these people were treated with anti-retroviral drugs, the mothers and fathers could raise their children, be out in the field growing crops, and so on.

What will it take to make a serious improvement in global health?

Right now, all the rich countries together give $6 billion a year in health aid to poor countries, out of a total aid budget of $50 billion a year. That total is two-tenths of 1 percent of their $25 trillion gross national product. The United States is the bottom in terms of aid per GNP. Our report calls for $27 billion per year in health aid alone to make a massive, needed attack on the disease burden.

What would that money buy?

Thirty to 40 dollars per capita would cover anti-retroviral therapy for AIDS, bed nets for malaria, monitored drug therapy for tuberculosis, vaccines, oral rehydration solutions for life-threatening diarrhea, antibiotics for acute respiratory infection, and midwives in attendance at childbirth. Such a program could save millions and millions of lives per year, with all the attendant economic benefits.

How do you make the case for funding health programs in poor countries while fighting terror is at the top of the U.S. agenda?

I'd argue there are huge social benefits for the rich countries as well, in not living in a world endangered by mass social instability, the spread of pathogens across borders, and the spread of all the other ills—whether it's terrorism, drug trafficking, or all the other calamities that accompany state failure.

You helped advise the economic transitions in Eastern Europe. How have those changes affected health?

There is a sharp divide between Eastern Europe and the former Soviet Union. Half of Poland's debts were canceled, and Poland had a significant improvement in health and life expectancy. But the West did not want to help Russia, so in the former Soviet Union there was a terrible health decline.

Overall, is global health getting better or worse?

There were remarkable gains in the 20th century: a marked increase of life expectancy and a marked decrease of infant and child mortality. There was also the expectation that we were on the verge of conquering infectious disease. Of course, with the AIDS pandemic, the resurgence of malaria and tuberculosis, and the emergence of new diseases, we have sobered up to the much deeper nature of the battle.

An extended version of this interview is available at www.discover.com.

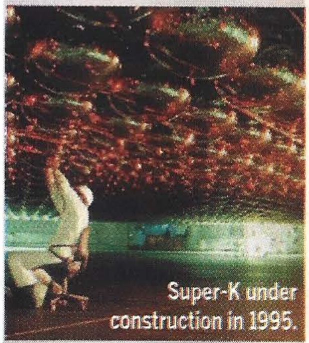
> 'Gravitation simply represents a continual effort of the universe to straighten itself out'
>
> *—Sir Edmund Whittaker*

FOLLOW-UP:

Who'll Watch the Neutrinos?

RESEARCH AT THE SUPER-KAMIOKANDE neutrino observatory in Japan ground to a halt last November after a routine cleaning ended in disaster. Workers were refilling the 135-foot-high water tank, which is lined with sensitive light-detecting tubes that pick up flashes triggered by neutrinos. When the tank was 80 percent full, roughly 7,000 of the submerged tubes imploded, leaving the detector crippled.

Officials at Super-K think insufficient padding placed on the bottom of the observatory may be to blame. Workers had to walk across this padding during cleanup and repair. Ironically, those footsteps probably weakened the tubes, leaving them unable to support the weight of the water when Super-K was refilled. The damage to the facility, which four years ago provided the first evidence that neutrinos have mass (see *Discover*, August 2001), is a major blow to particle physics research. Super-K director Yoji Totsuka says the facility will resume limited experiments by the end of this year, utilizing its remaining 5,000 tubes. But getting back to full strength may take four years and $20 million. *—Maia Weinstock*



Super-K under construction in 1995.

PHOTOGRAPH: RIGHT, COURTESY OF KAMIOKA OBSERVATORY/ICRR/UNIVERSITY OF TOKYO.

AM 530 600 700 800 1000 1300 1600 kHz
SW1 3.2 3.6 4.2 6.2 7.0 7.6 MHz
SW2 9.2 10.6 12.2 17.8 20.0 22.6 MHz
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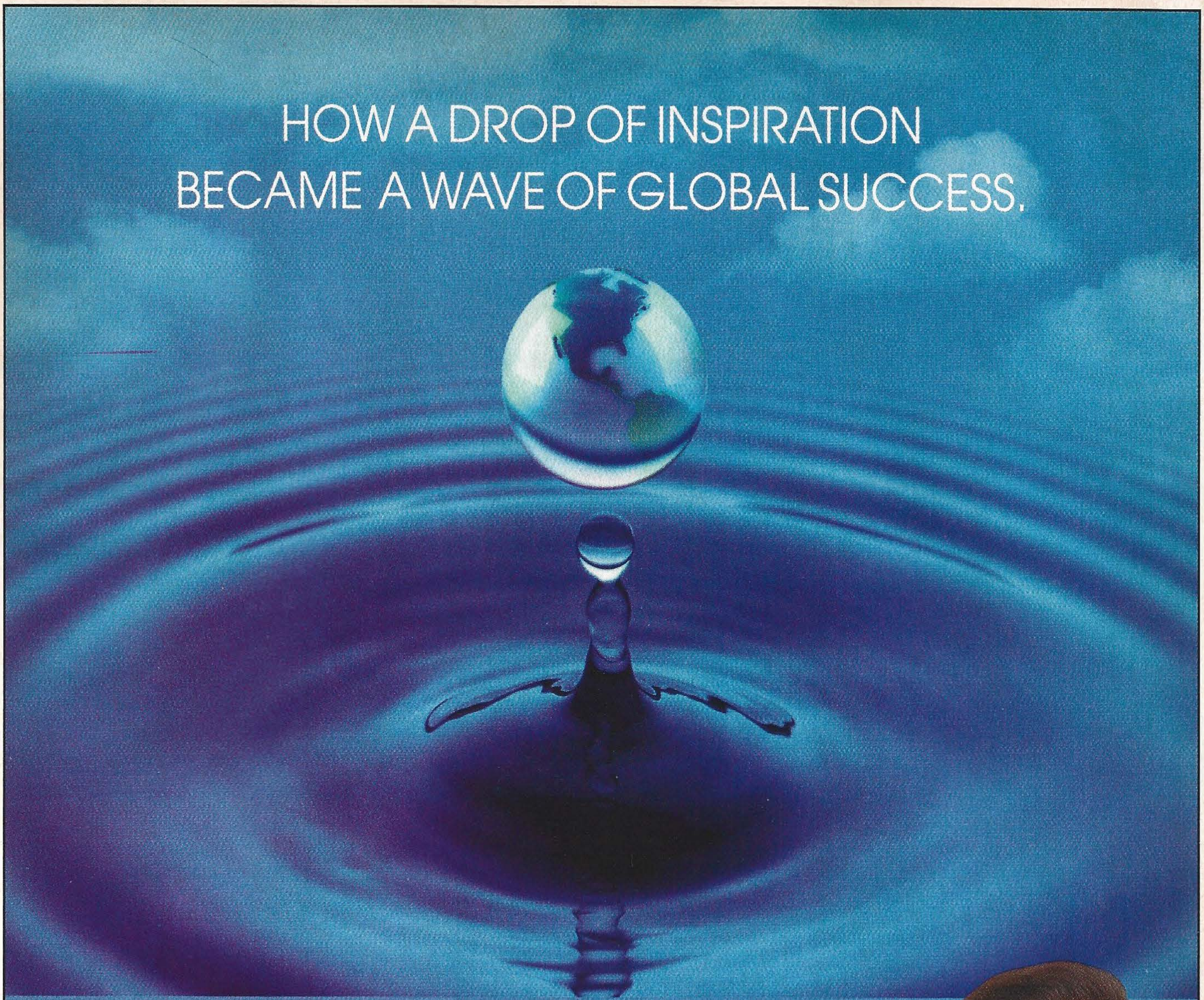
HOW A DROP OF INSPIRATION
BECAME A WAVE OF GLOBAL SUCCESS.

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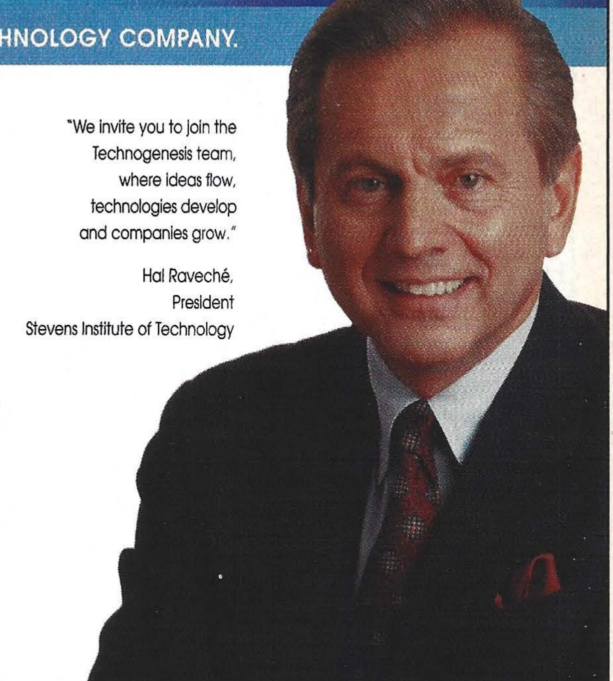

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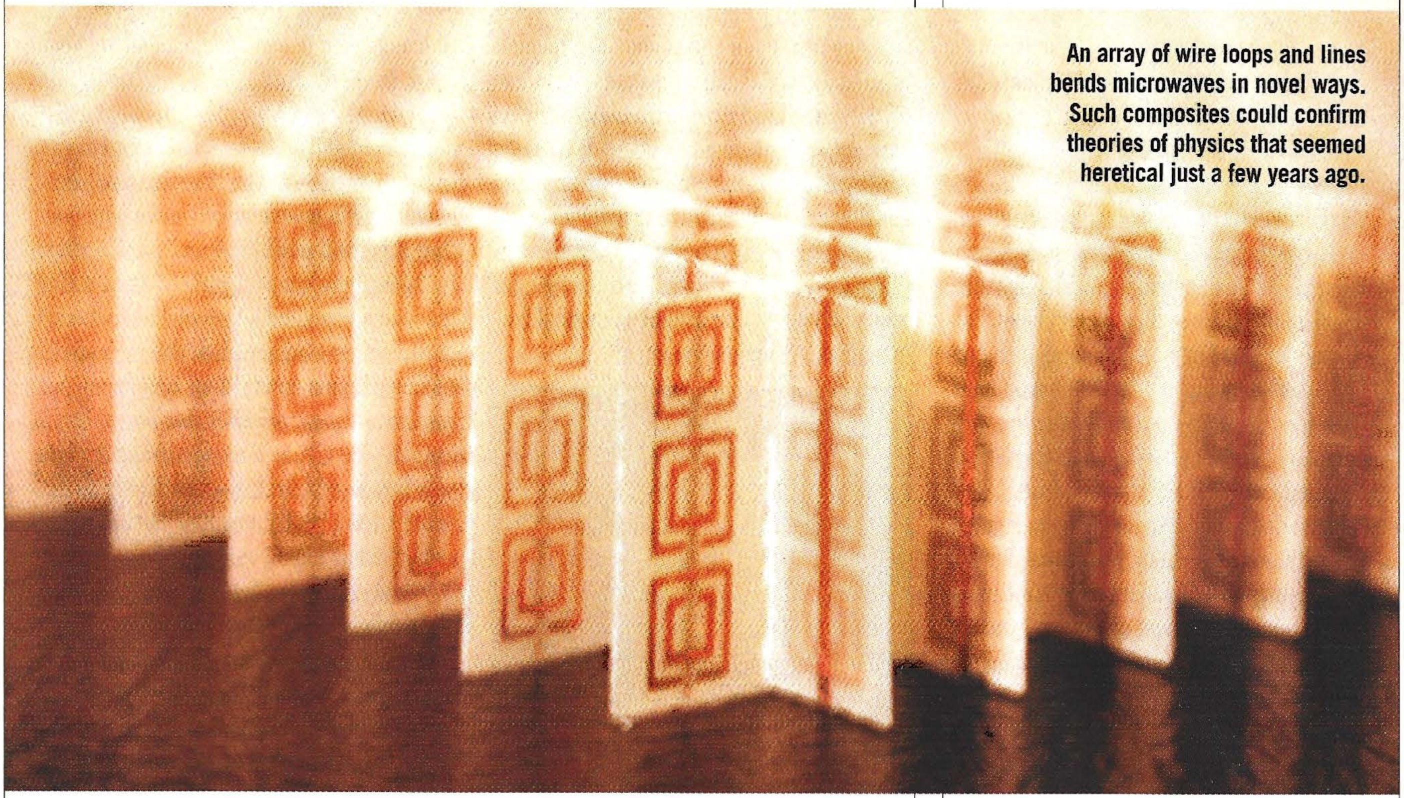


An array of wire loops and lines bends microwaves in novel ways. Such composites could confirm theories of physics that seemed heretical just a few years ago.

PHOTOGRAPH COURTESY OF DAVID R. SMITH/UCSD.

Scientists reverse the laws of optics in a quest to create the perfect lens

Through the Looking Glass

"EVERY DAY YOU PLAY WITH THE LIGHT OF THE UNIVERSE," WROTE CHILEAN POET PABLO Neruda. Physicist David R. Smith of the University of California at San Diego takes those words to heart. He spends his days contemplating how to bend light in ways that reverse the normal patterns of refraction. And his are more than theoretical musings. Smith and a handful of like-minded researchers are now building mirror-image materials that could ultimately result in practical applications ranging from better cell-phone antennas to DVDs that could cram 100 movies onto a single disc.

These playful manipulations of light were anticipated by the long-neglected ideas of Soviet physicist Victor Veselago of the Russian Academy of Sciences in Moscow. In 1964 Veselago theorized that the laws of physics allowed for the creation of a material that he described as "left-handed" because of the way it would affect light or other radiation passing through it. In conventional materials a ray of light moving forward has an associated electric field that points left and a magnetic field that points up. You can picture this arrangement by pointing the thumb, forefinger, and middle finger of your right hand in mutually perpendicular directions. In Veselago's bizarre material, these orientations would be mirror reversed, so they would follow the pattern of the fingers on the left hand instead.

This seemingly simple change would lead to some very peculiar consequences. Perhaps the most surprising one is a negative index of refraction, the measure of how a given material bends light. Glass, water, and every other known substance have positive indices of refraction. That is why a swimming pool looks shallower than it really is and why sunlight comes to a point when it passes through a magnifying glass. A left-handed magnifying glass, by contrast, would disperse light, while a concave lens or even a flat piece of left-handed material would bring light to a focus. All most strange. But Veselago had no notion of how to make such a material, so his work languished in obscurity.

Three decades later John Pendry of Imperial College in London recognized that even though left-handed materials don't exist in nature, it might be possible to construct composite structures, or meta-materials, that have left-handed traits. The building blocks of such meta-materials would be small metallic structures that collectively respond to electricity and magnetism in novel ways. For instance, the electric charges within a substance normally try to align themselves with an applied electric field. But in an array of thin, conductive wires, the surface electrons are sluggish and respond out of step so that the charges oppose rather than align with the electric field. In 1999 Pendry and his →

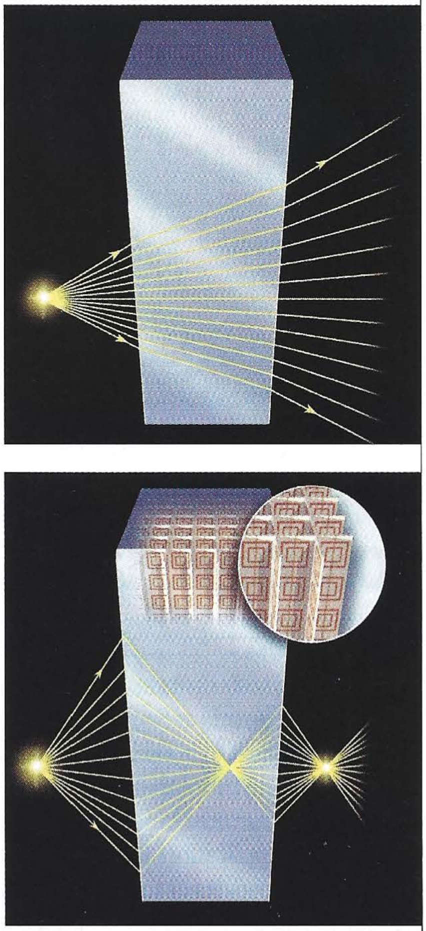
Left-handed material reverses all sorts of optics rules. Its Doppler shift is inverted, like an ambulance wail that gets lower rather than higher in pitch as it approaches. Even stranger, it makes the energy within a beam of light appear to move in the direction opposite to the beam itself.

→ colleagues at Imperial College and Marconi Caswell Limited, in Northamptonshire, England, performed calculations showing that a split ring of metal—a hoop with a small gap in it, like the letter *C*—could exhibit a similarly reversed response to magnetism.

Two papers describing this work caught the eye of Smith and Sheldon Schultz, another physicist at the University of California at San Diego, who set out to create a full-blown left-handed material. They found that a double split ring, one metallic hoop nestled inside the other, worked even better than a single ring. After some experimentation, Smith, Schultz, and graduate student Richard Shelby imprinted an array of split rings in copper film on one side of a standard fiberglass printed circuit board. Then they added an array of parallel metal wires on the other side. Together, the rings and the wires inverted both the electrical and the magnetic properties of the light. Finally, the researchers slotted the boards at right angles, like the cardboard compartments in a crate of wine, to create a left-handed prism.

The next step was to test whether the material would bend light waves the way Veselago imagined. The split-ring design works only on wavelengths longer than the size of the rings, which are about one-fifth of an inch wide. That is far longer than visible light; it is the wavelength of microwaves. So the researchers passed a microwave beam through their meta-material to explore its properties. Last spring they reported their results: The bending of the microwaves indicated a negative index of refraction as large as –2.7.

The result came soon after the Defense Advanced Research Projects Agency decided to fund research to develop meta-materials "with superior microwave and/or optical properties for communication, radar, and wireless power transfer application." The left-handed materials created by the San Diego research team fit the bill. "Meta-materials with a negative index of refraction may reduce the cost and improve the performance of many devices used in wireless communications," Smith explains. He and his colleagues are also working with Lucent Technologies to explore ways to make antennas that can handle high data-transmission rates. Because of their inverted properties, left-handed materials might make it possible to place multiple antennas close together while generating only minimal interference. "We have not even begun to tap the applications at microwave frequencies, let alone what may lie ahead at optical frequencies," Smith says.



A pane of normal, right-handed material (top) slightly disperses light. Left-handed material (bottom) brings the rays to a focus. A flat slab of such material could, in principle, act as a super-microscope.

Pendry already has a vision of what a visible-light left-handed material might do. He has shown that it could act as the perfect lens. Conventional lenses cannot reveal any detail smaller than the wavelength of light they are focusing, so they hit a wall of resolution at several hundred nanometers, about 1/100,000 inch. This limit applies to all light that is propagating through space. But strange as it seems, not all light propagates. There is also a stationary electromagnetic glow, known as the near field, surrounding all light-emitting or light-reflecting objects. The near field contains the fine detail that is normally lost from the image, but it is so narrow—just a few tens of nanometers—that it is inaccessible to ordinary optics. In 2000 Pendry recognized that a flat lens composed of left-handed material could focus and amplify the near-field radiation and so yield an image whose resolution is far smaller than one wavelength. Last year's experiment by the San Diego research team affirmed that such a lens really could exist, for microwaves at least.

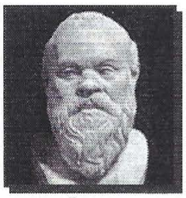
What engineers really crave, however, is a perfect lens that bends visible light. Then they could etch much smaller circuits onto computer chips, or burn many more spots of data onto a single DVD, or study now-invisible physical processes that occur on the surfaces of materials. To meet such a challenge would require shrinking the components of the left-handed material by a factor of 10,000 or more. Smith explains that his research team's design won't work for wavelengths shorter than infrared because the electrical properties of the metals change at smaller scales. "There is as yet no optical analogue for the material we developed," he says.

Photonic crystals—a class of composite materials whose basic building blocks are microscopic spheres—might be able to provide a negative refractive index for visible light. "But this effective negative refraction doesn't appear to have the same remarkable properties with respect to the near field, so the prospects for optical versions aren't clear," Smith says. Pendry is moving in the other direction, developing a rolled-up meta-material that bends long-wavelength radio waves. He hopes to use it to focus the waves that are used to form images in MRI scanners so that doctors can zero in on one small region of the body.

Even as he contemplates practical applications, Pendry is still amazed that nature allows the left-handed world to exist at all: "People have been surprised by this behavior, and that includes myself. Sometimes I feel like a heretic." ☒

GRAPHIC BY MATT ZANG

Let their lives be your teachers . . .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by jocelyn selim

The clue to understanding anxiety may be written in your genes

The Sum of All Fears

WHEN CHARLES DARWIN RETURNED TO ENGLAND IN 1836 AFTER HIS FIVE-YEAR VOYAGE ON the *Beagle,* he was 27 years old and on the cusp of one of the most brilliant careers in the history of science. He was also a bit of a wreck. He began complaining of "constant attacks"—heart palpitations, trembling, shortness of breath, and "swimming in the head." When offered a secretaryship at the Geological Society of London, he declined, explaining that "anything that flurries me completely knocks me up afterward." Two years later the once-intrepid traveler moved to his country home in Kent and became a legendary recluse, leaving only when absolutely necessary and then traveling in a carriage with darkened windows. On one rare trip in 1861, a brief speech in front of the Linnean Society prompted a 24-hour vomiting episode.

Darwin never learned the true nature of his malady. Physicians of the time diagnosed it as anything from "dyspepsia with aggravated character" to "suppressed gout"; their successors might have attributed it to a weak nervous system or a conflicted superego. But according to a team of researchers led by Xavier Estivill, a molecular geneticist at Barcelona's Medical and Molecular Genetics Center, Darwin's agoraphobia may have had a more specific origin. In a study published in the journal *Cell* last summer, Estivill contended that nearly every social phobia and panic disorder is rooted in a single stretch of about 60 genes.

Anxiety disorders first caught Estivill's attention 14 years ago through the work of physician Antoni Bulbena. While working at the Hospital del Mar in Barcelona, Bulbena made an odd observation: Patients who were double-jointed complained of nervous disorders far more often than others—fully 16 times as often, a follow-up study showed. Intrigued by the coincidence, Estivill traveled to a small Catalonian village near Barcelona, collected DNA samples from families known to have both conditions, and began combing through the samples for common characteristics.

Such comparative research usually entails a genome-wide analysis—an onerous process of lining up corresponding segments of DNA and looking for shared sequences. But Estivill, on a hunch, took a shortcut: He first examined the blood and then the sperm cells of 10 of the patients for genetic abnormalities that might contribute to the association. It was on the 15th chromosome that he found what he was looking for: Eighty-seven percent of the double-jointed and 90 percent of the anxiety-afflicted villagers carried a duplicated region spanning the length of about 60 genes. When Estivill repeated the study in a group of unrelated Catalonians, the association was even stronger: Ninety-seven percent of those diagnosed with an anxiety disorder carried the duplication compared with 7 percent in the general population. "It was astounding," he says. "You just don't expect that much of a relationship between a single region and a complex disorder that's supposed to be the result of many genes."

If Estivill's numbers hold up, says University of Oxford molecular biologist Jonathan Flint, they will demonstrate the most specific genetic association ever reported for a psychiatric disorder. "It's got a lot of people excited," Flint says. Like many of his colleagues, however, Flint still has nagging doubts. During the past year alone, he notes, an average of one study a day has been published purporting a genetic link to some psychiatric illness or other. Granted, no other study has produced statistics so compelling, but if the link was so obvious, why had no one found it before?

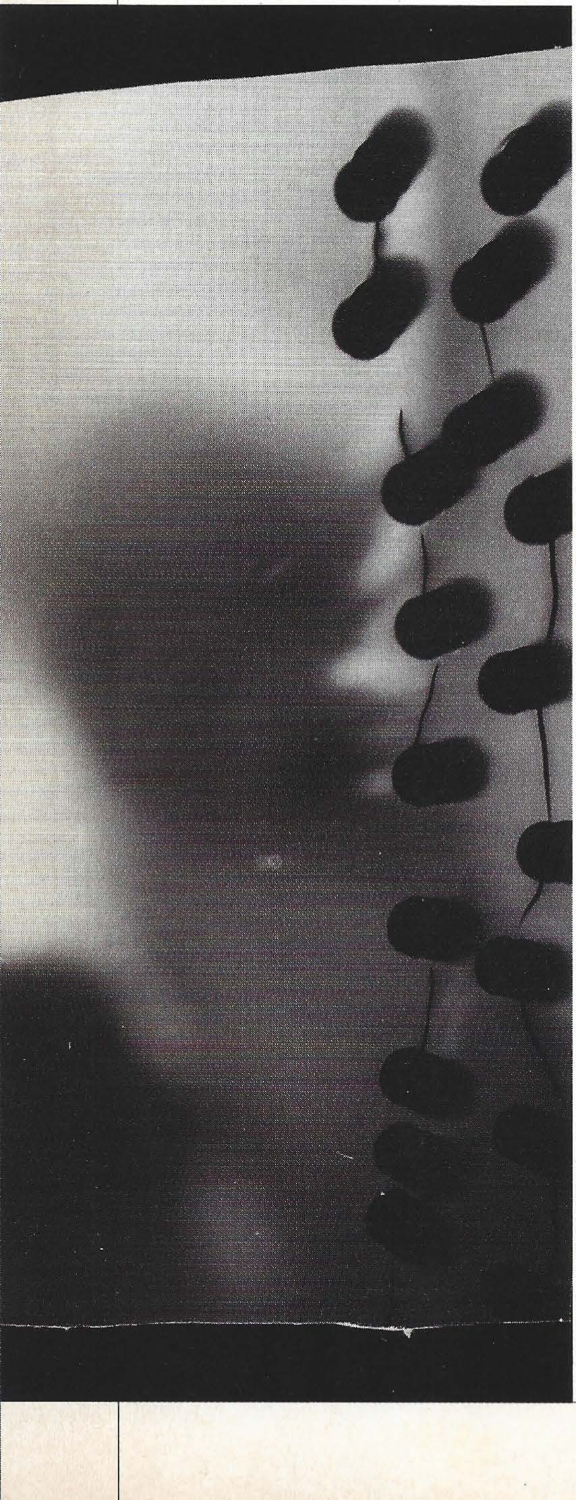
The answer, Estivill says, is that the duplication isn't being passed along ac-

Phobias and panic disorders affect as many as 1 in 10 people and cost tens of billions of dollars in treatment and lost productivity. In the United States more than 30 percent of all apparent heart-attack patients who use emergency services are actually suffering from panic attacks.

PHOTOGRAPH BY GERALD SLOTA/RICCO/MARESCA GALLERY

cording to standard patterns of heredity. Most other genetic disorders are caused by a hereditary mutation at a specific location on a specific chromosome. Cystic fibrosis, for instance, is caused by a mutated gene that codes for a faulty protein that makes the mucus in the lungs too viscous. Such genes might be dominant or recessive, but once they appear in the DNA, they are passed down through the generations virtually unchanged.

Estivill's duplication doesn't work that way. Not only does its position change along the chromosome, but its sequence is sometimes inverted or otherwise rearranged. Stranger still, those changes sometimes occur from cell to cell in the same individual, not just between parents and offspring. The reason, Estivill suggests, is that the duplication itself isn't being passed along. Rather, it's the *tendency* to duplicate that's inherited.



There are two ways such a pattern of inheritance could occur, he says. The enzymes that repair or copy DNA could be faulty and more prone to making doubling errors. Or the problem could have a more novel origin. The 60-gene duplication area is surrounded by smaller repeated sequences known as duplicons. Such duplicons are usually just junk DNA, but under certain circumstances they could cause trouble. "If the smaller repeats are very close copies of each other, they could throw off the copying machinery—trick it into making it see something twice and make a double copy of a nearby region," Estivill says. "It's impossible at this point to say exactly how this is happening. You've got to keep in mind that this is something no one has ever seen before."

In essence, Estivill is proposing an entirely new mechanism of genetic disease. "It's not an unreasonable explanation, given his observations," says Brad Schmidt, a psychologist at Ohio State University's Anxiety and Stress Disorders Clinic who has been looking for anxiety-related genes for nearly a decade. "I have a hard time believing something that looks as complex as panic disorder and phobias could really be that simple, but then the history of science is full of cases that looked very complex from one angle and turned out to be very simple when viewed another way. We've assumed that because drugs like Xanax and Paxil are so effective, all sorts of combinations of genetic variants of their receptors must play a role. But that line of thinking might be right up there with assuming that an aspirin deficiency causes arthritis."

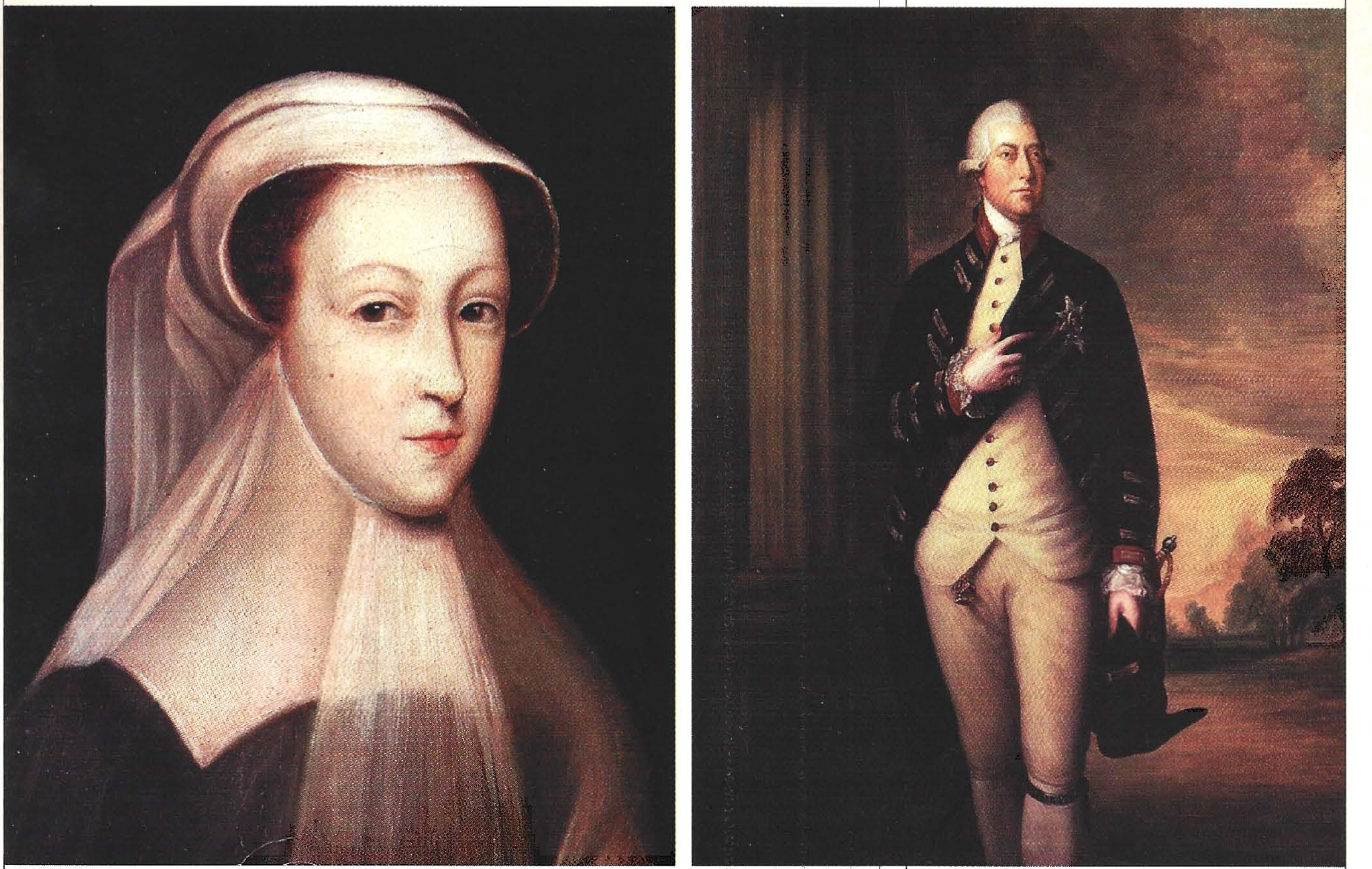
If Estivill is right, such chromosomal rearrangements could lie behind many other hereditary disorders—schizophrenia, obsessive-compulsive disorder, and depression among them. Or for that matter, patterns like the duplication could cause any illness—from asthma to heart disease—that has been blamed on the effects of many genes working in concert. So far, attempts to unravel the genetic basis of complex conditions have been embarrassingly unsuccessful, Flint admits. "When attempts to find particular combinations of genes fail, the common wisdom just assumes they are even more complex than anyone thought. A mechanism like Estivill's could potentially explain quite a lot."

Since isolating the duplication region, Estivill has gone a step further, pinpointing his patients' anxieties to a double dose of at least one neuroreceptor coded for by one or more genes. "We can't be certain. We haven't identified all the genes in the region," he says. "But this one is a type thought to play a central role in the brain regions activated by fear." Mice that Estivill has bred with an extra copy of one gene scare more quickly and run away faster when faced with rats, bright lights, and other mouse horrors.

Such discoveries may well lead to treatments for anxiety disorders, but an outright cure would be going too far. Unlike hemophilia, Huntington's disease, and other hereditary illnesses, a certain amount of anxiety is good for people. "It's part of a highly evolved and adaptive defense mechanism and protects us from getting too close to cliff edges or hungry lions, just as the immune system protects us from bacteria," says Randolph Nesse, an evolutionary psychiatrist at the University of Michigan. Panic attacks are less a problem of maladaptation, Nesse says, than a case of too much of a good thing.

Even Darwin recognized that his suffering had some benefits. Before he died, he admitted that "ill-health, though it has annihilated years of my life, has saved me from the distraction of society and its amusements." Without panic disorder to focus his passions and spare him from interruptions, some researchers have suggested, Darwin might never have written *On the Origin of Species.* ☒

by pamela grim



Mary Stuart, Queen of Scots (left), may have suffered from this rare ailment. A more certain diagnosis was made in one of her descendants, King George III (right).

Uncovering a rare but age-old disease of pain and madness

Why Does This Belly Ache?

THE YOUNG MAN'S MOTHER SAID, "HE GETS LIKE THIS."

"Like what?" I asked.

"Pain. He gets this pain in his stomach, and then he gets like this."

She was a country woman, shy with doctors. She wouldn't look at me as she told her son's history. He was 22 and clearly in pain. From the moment he stepped into room 7, I could hear him wailing and moaning.

The problem was that somehow it just didn't seem real. While the nurse was trying to start an IV, he lay there acting as if he were being nailed to a cross: "They're killing me."

The nurse's note was to the point: "History of abdominal pain, now with same, only worse." I laid my hands on the young man's abdomen and wasn't surprised it was soft. Nothing there.

I continued the exam, his mother regarding us both. "He gets real constipated," she said, "and then he gets strange in the head. Sometimes he doesn't make a lick of sense." She searched for a moment and then found the correct word. "Peculiar." She looked as if she had had about enough.

"How long has he had this pain?"

"Oh, couple a years. Off and on."

"Has he seen a doctor about it?

"He's seen pret' near every doctor, and they say pret' near the same thing: Don't know."

Chronic belly pain is a vast wasteland of diagnostic dead ends. Test after test can send a physician back to the beginning. Even the best of them often come up with nothing more definitive than dyspepsia, Latin for "bad digestion."

"Your son ever seen a psychiatrist?"

"He's seen a couple . . ."

"What did they say was wrong?"

"Well, they said different things. One doctor said he was depressed, and another doctor said he had an anxiety problem. And one doctor just told me his problem is all in his head."

I noticed something that didn't fit. Sweat was beading on the man's forehead and upper lip. If you're just looking for attention, that's hard to fake.

In most countries, roughly one out of 100,000 people has a problem with one of the eight enzymes that assemble heme, the oxygen-carrying component of hemoglobin. The symptoms, which often don't show up until after puberty, can be aggravated by exposure to some foods and chemicals.

PHOTOGRAPHS FROM ARCHIVE ICONOGRAFICO, S. A./CORBIS (2).

Sometimes when I am stumped for a diagnosis, I try to simplify as much as possible. How would I describe this case in a few words? Well, it would be belly pain and craziness. Delirium would be the medical word. So what would cause belly pain and delirium?

I had the image suddenly of a man running down the hallway in his white nightshirt, raving like a madman—King George III of England.

Porphyria. The king had porphyria.

Porphyria is a family of diseases, rare diseases, several of which manifest as gastric symptoms and mental-status changes. Some historians think King George, who would dash naked down the castle halls while his ministers and advisers chased frantically after him, was a victim of porphyria.

I tried to remember what you do if you suspect porphyria. This is not a disease emergency room doctors diagnose every day, except in South Africa, where, because of a genetic fluke, it's common in the Afrikaner population. I looked at the young man and wondered if he could be of Dutch descent.

"Does his urine ever get dark?" I asked the mother.

The mother drew back. "Well," she said, "I don't know. He drinks a lot of pop."

I had seen a urine specimen from him. I found it, still waiting to be tested, by the vacuum tube.

I remembered that before you diagnose porphyria, you must test the urine. But test it for what? Pigments, I remembered; you test for pigments. Pigments are molecules that love light. With that in mind I held the patient's urine up to the light to examine it.

I saw a weird color, a brilliant burgundy, oxblood red. More telling was a faint strip of deep-water blue up near the surface.

Porphyria comes from the Greek word for purple. All porphyrins are pigments. They function as energy transporters in many systems and are also involved in the assembly of the oxygen-transporting component of hemoglobin, the heme, in our blood.

For most people this system works just fine. Occasionally, though, one of the enzymes involved in making heme molecules is defective or disabled. In that case half-baked, not-quite-heme molecules pile up. Porphyrin molecules and their precursors begin to spill into the bloodstream and out through the kidneys into the urine. Eventually, the cells that manufacture heme begin to malfunction, and biological chaos ensues. The result: symptoms of porphyria.

By some whim of nature, the organs primarily affected by the disease are not the liver or bone marrow cells but the nervous system and the skin. With skin involvement, just a brief stroll in the bright sun produces major skin injury. Nervous system involvement produces sensory changes, paralysis, madness. Abdominal pain is a common symptom, but the abdominal organs aren't directly involved. The symptoms come from madly misfiring neurons that activate the pain receptors lining the abdominal cavity.

King George III of England suffered from intermittent bouts of madness, now thought by some to be secondary to porphyria. He developed his first episode when he was in his twenties. They were classic: abdominal pain with severe constipation and delirium. His doctors were baffled both by his symptoms and by the results of one of the few tests they could do: a detailed inspection of the king's urine. In times of madness, they wrote, his urine was "sometimes wine dark and sometimes deep blue." We now know this was the shimmery blue of dissolved porphyrins.

The king went mad, recovered, lost an empire, went mad again, recovered, and finally died mad, leaving behind the mystery of his blue urine.

I thumbed through an old textbook to find what diagnostic tests I should order: 5-Aminolevulinic acid, ALA for short, and porphobilinogen.

I ordered the tests. Then I did what people in the emergency room always do when a strange case like this comes up: I forgot all about it. Other dramatic cases showed up. There was a sexually abused 10-year-old girl and a baby born in the ER parking lot.

I would never have known this patient's diagnosis if I hadn't called his doctor a week later about a different patient.

It was early in the morning, and I had called to admit an asthmatic patient. The doctor asked me sleepily, "Do you remember that patient . . . that kid you admitted last week? Well, you were right. The kid has porphyria. Somebody should have picked it up long ago." He said the patient might be able to control the symptoms through changes in diet. But porphyria comes in several varieties, he added, and the young man's treatment would depend on what type he had.

THE KING WENT MAD AND DIED, LEAVING BEHIND THE MYSTERY OF HIS DEEP-BLUE URINE

Driving home that morning, inching along in rush-hour traffic, I had a vivid vision of myself. I was a giving a lecture on porphyria, presenting my patient to an audience and explaining the biochemistry of porphyria. I was going through the metabolic pathways of heme synthesis, using a diagram detailing the steps in porphyrin's synthesis. I was explaining all this and knew I was doing a great job. When I turned around to address the audience, though, I found it was not made up of doctors but of patients—all with belly pain. Everyone looked sick and worried. Everyone was pointing to his or her own abdomen. Then each said the same thing in one unified voice: "OK, OK, so you diagnosed a case of porphyria. But what I want to know is, What about me? What's my diagnosis?"

That's when I realized I hadn't a clue. ☒

THE DOCTOR IS IN

Pamela Grim is an emergency room physician at Geauga Hospital in Cleveland, Ohio. "This was an unusual diagnosis to make in the ER," she says. "We don't have the mind-set of vanishingly rare chronic diseases." Grim's stories about emergency room medicine, *Just Here Trying to Save a Few Lives,* is just out in paperback.

The case described in Vital Signs is based on a true story. Some details have been changed to protect the patient's privacy.

by karen wright

Forget mice, what scientists need are *Drosophila,* lots of them

Flies 'R' Us

AFTER THREE DECADES OF STALKING FRUIT FLIES IN THE WILD, THERESE MARKOW HAS HONED her technique to a fine art. Her weapon is a long glass tube with a gauze trap in the center. "You sneak up on the flies and suck," she says. "Then you blow them out into a vial."

Most folks would just grab a flyswatter. But Markow is charged with keeping fruit flies alive and thriving—not the dozen or so that might hover over a black banana on the kitchen counter but the thousands, maybe even millions, housed at the National Drosophila Species Stock Center at the University of Arizona in Tucson. As the center's director, Markow presides over an invaluable scientific resource: a collection of some 270 species and 1,500 strains from the family Drosophilidae. Fruit flies are the preferred pet of scientists studying topics from alcohol intolerance to the origin of species. Markow's flies were culled from their native habitats around the world, and more than 1,000 orders are shipped out each year to equally farflung laboratories. For $20 to $75 a pop, researchers can procure by express mail a sample of the living descendants of, say, one *Samoaia leonensis* collected from Afiamalu Road in Upolu, Western Samoa, on July 22, 1967.

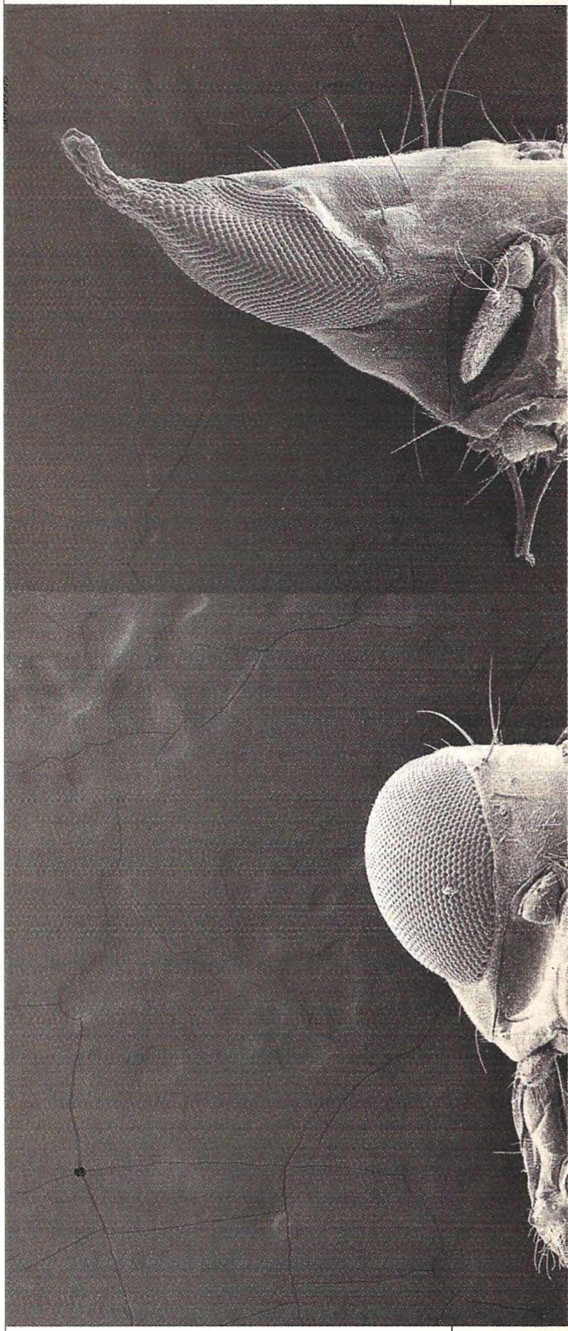
"There are actually a lot of important issues addressed by flies," says Markow, who is also a professor of ecology and evolutionary biology at the university. "It's not just a bunch of bugs."

A century ago fruit flies *were* just a bunch of bugs, albeit a diverse and robust bunch. A few thousand species live on six continents, from the tropics to the northernmost temperate zones. Ironically, some of the species are finicky eaters that don't like fruit at all: They live exclusively on cacti or mushrooms or flowers or the larvae of other insects. Other species, including the one circling the bananas, are no more particular than houseflies. It was one such common pest that a Harvard geneticist named William Castle caught in 1900 for one of his student's experiments. The animal's appeal—in fact, its only appeal—was expedience.

"A half-pint milk bottle with a piece of rotting banana would keep two hundred flies happy for a fortnight," writes evolutionary biologist Martin Brookes in *Fly: The Unsung Hero of 20th-Century Science.* "They were also easy to breed, with each female laying several hundred eggs. . . . [B]irth, sex and death were all wrapped up inside a few tumultuous weeks. In short, fruit flies did pretty much what other animals did, only cheaper and faster."

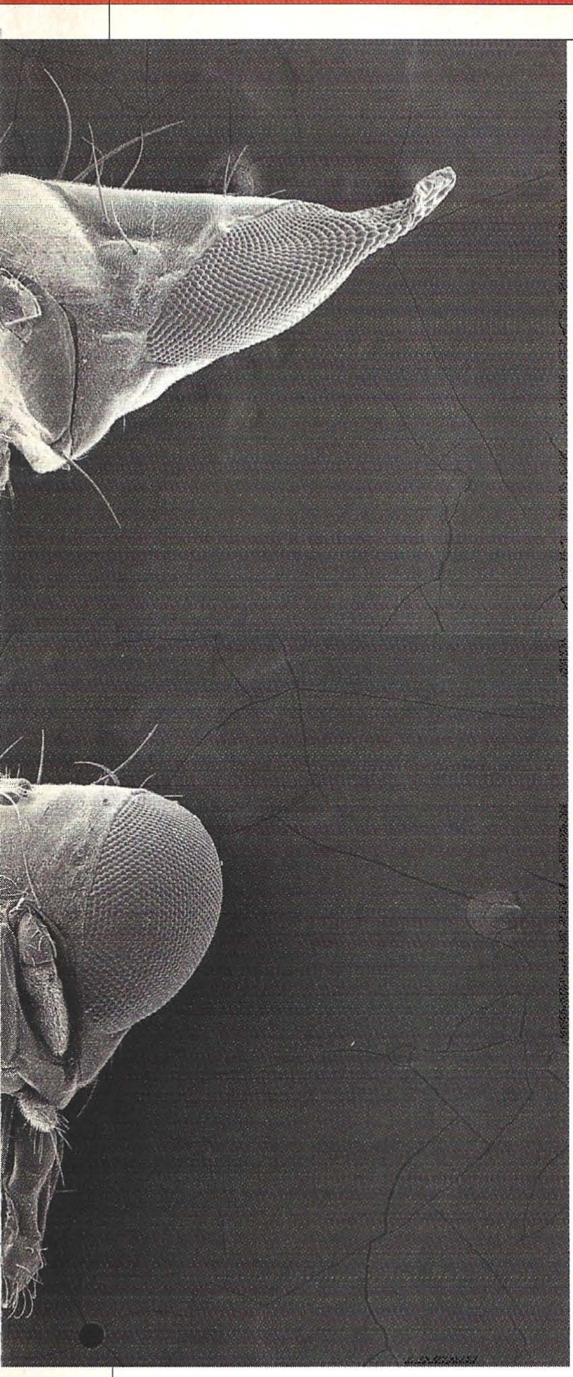
The brevity of the fly's life span made it an obvious candidate for studies of genes and evolution. By the middle of the last century, one species, *Drosophila melanogaster,* was de rigueur in genetics labs, where it helped to prove, for example, that microscopic structures called chromosomes contain the hereditary molecule called DNA. The chromosomes of *Drosophila* larvae are unusually thick and distinctly banded, so researchers can easily detect genetic deletions and rearrangements under the microscope. When molecular biologists learned how to manipulate genes, tinkering with fruit flies revealed how a complete organism emerges from a simple fertilized egg. The genes involved are remarkably similar in a host of animals and have yielded many insights into human development as well.

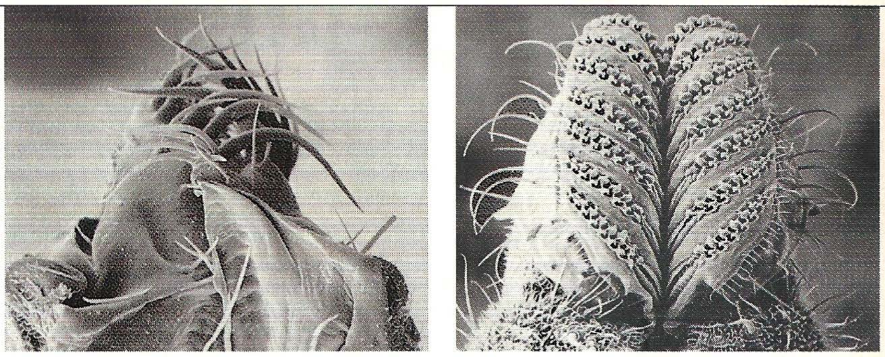
While lab-bound biologists messed with *D. melanogaster*'s genome, those with a flair for adventure went looking for the experiments that had already been conducted in nature. Beginning in the 1920s, a handful of researchers began combing the globe for new fruit-fly species they could compare with the familiar *D. melanogaster.* They found a seemingly endless variety of adaptations among the flies: Some can live on toxic fungi or rotting grapes with dangerously high alcohol levels. Some live in cactus plants that endure the temperature extremes of the desert. Many of the species are so specialized that they can't be bred in captivity. But collectors brought home as many as they could and eventually pooled their informal stocks into the federally funded collection in Tucson.



PHOTOGRAPHS BY DAVID GRIMALDI.

Residents of the National Drosophila Species Stock Center live in glass vials with cotton plugs in a suite of small rooms on the University of Arizona





Left: Some male fruit flies from the South American genus *Zygothrica* (top left) have heads shaped like anvils, which they deploy in fights with other males. Females of the genus have ordinary round heads (bottom left). Above: Even the tips of the proboscis, which is used for feeding, can vary widely among fruit-fly species.

campus. A staff of about 10 cooks and cleans for the flies, which are fed from a menu of six special blends based on bananas, cornmeal, potatoes, prickly pear cactus, flower nectar, or a high-protein mix made from brewer's yeast, wheat germ, and baby food. Many of the flies are destined to become world travelers. Some will end up at La Trobe University in Australia in the laboratory of Ary Hoffmann, who compares heat tolerance among different species to understand the physiological and molecular basis for evolution. At the University of Wisconsin, Sean Carroll uses fruit flies to map the genes responsible for body color, which plays a role in courtship, camouflage, and temperature regulation. "This whole flock of *Drosophila* species that's available because of decades of work helps us to understand the genetic architecture that underlies structural differences between species," Carroll says.

Markow moves between the center's collections and the Sonoran Desert to track the rise of new fruit-fly species in the wild. "The diversity in all of these things is really what makes them so attractive," she says. "We find a huge variation in this genus, and I want to know where it comes from."

While the flies at the center are thriving, their curators have become something of an endangered species. When Markow took over the collection two years ago, she decided to do an overhaul of the stocks, making sure they were properly cataloged and cared for. To her dismay she soon discovered that the experts capable of identifying Drosophilidae members—most of whom were the original collectors—were themselves in short supply. "The people who described all the species when they were discovered in the 1940s and 1950s are all retired or dead," she says. "Nobody wanted to sit and look at fly pee-pees to tell them apart."

Yet "pee-pees" are indeed the only way to distinguish among many species of fruit fly. Even under a microscope, Drosophilidae females may look identical to all but male fruit flies, and while males sometimes have unusual heads (one is anvil-shaped, like a hammerhead shark), the most telling differences occur at the other end. "They have incredibly complicated genitalia, but it's all accessory parts," says David Grimaldi of the American Museum of Natural History, one of the few entomologists with the requisite skills. "They have little corkscrews and stuff. There's one that looks like a huge, erect human phallus. You wonder how they copulate with these things."

As one her first directives, Markow organized a gathering of learned elders last fall to train a new generation of scientists in the almost-lost art of Drosophilidae identification. The reunion drew plenty of interest from young colleagues as well as enthusiasm from the old school. "These guys hadn't seen each other in years," says Markow. "They've forgotten more than we'll ever know." A dozen students spent two days bent over microscopes with the world's expert knowledge at their disposal. In the smallish world of fruit-fly caretakers, the conference was a historic event.

Tom Watts, Markow's lab manager, was in attendance. "It was like the Jedi Knights came to town," he says. ☒

The National Science Foundation supports 17 living stock collections that maintain organisms for use in research. Their stocks range from bacteria to primates. One center in Bloomington, Indiana, is so specialized it houses only varieties of *Drosophila melanogaster*.

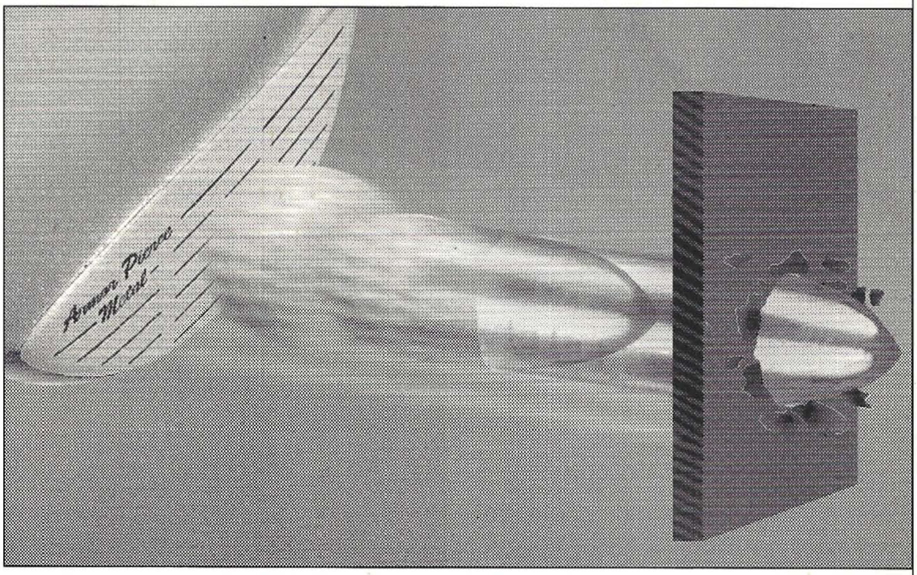
ADVERTISMENT

SPORTS TECH NEWS–2002

New golf club's secret metal hits too far on some par 4's.

Metal created by Department of Defense for tips of torpedoes and shells

How to win a long-ball contest



Once-secret Armor Pierce Metal was developed by the military for the tips of shells and torpedoes. On the face of a golf club the metal's extreme hardness adds significant yardage to a golf shot.

by Charlie Allen

YALESVILLE, CT-A once-secret metal used to penetrate enemy armor is now helping golfers hit very long shots. The metal-- a combination of ceramic, tungsten and four other materials-- was necessary because steel and titanium are too soft to pierce modern-day armor.

Now, an ex-Navy engineer working with a small golf company in Connecticut has applied the metal to the face of a driver, and some strong golfers are hitting shots so far they have to use the 3-wood on par-4's to avoid over-hitting the green. For instance, a PGA professional who played a round with the new driver told me he had to use the 3-wood on 300 to 330-yard holes to keep the ball from flying over the green. Here are more stories that help illustrate the club's potential power.

A golfer in California, after 40 years of golf, won his first long-ball contest using the club. Another shot his first sub-par round in 20 years. A golfer handicapped with an artificial leg out-hit his pro with a 320-yard drive and cut six strokes off his score.

Two broken balls-- two long-ball wins

At a driving range, a golfer using the new club was hitting the ball so far others had to try it. Everyone out-hit their own driver, including a young man who had just bought a new $400.00 titanium driver. Another golfer, a long hitter surely with some help from the wind, hit a 420-yard tee-shot. That exceeds the average drive on the PGA Tour by over 150 yards.

Another hit shots so hard he split a balata ball and a Surlyn-covered Titleist. He destroyed two balls, but he won two long-ball contests.

A Director of the company that markets the new driver told me this.

"Twenty-three years in the business and I have never seen shots hit so far. This new Armor Pierce Metal clobbers balls like a battering ram. There is virtually no loss of energy at impact. All the juice goes into the ball. At high club-head speeds, it can actually break balls! And it's easy to control.

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"A well-known professional we know tested the club for us during a tournament warm-up and was curling 300-yard shots around trees with such accuracy several of his peers wandered over to try it. They were awed. But for their contracts, seven top pros could have been playing our Controller Driver in a national tournament that day. We would have sold thousands.

"The Controller Driver's control comes from probably the biggest, most forgiving sweet spot in golf-and a scientific roll and bulge that tames hooks and slices. A good golfer can draw and fade shots just like our famous friend.

"An independent lab found that these features keep tee shots 78% closer to the centerline than a leading tour driver. We found this so startling we asked an outside consultant to test it among a group of real-life golfers. The results were just as startling. They landed four times--four times--as many tee shots within ten yards of the centerline with the Controller Driver than with their own drivers.

"The club's dynamite. We know of no other driver that can match its power."

The Controller Driver's head is about the same size as the Great Big Bertha titanium driver and its shaft is 45-inch long for extra club-head speed.

If you want to try it on the course on in a long-ball contest, the maker, NGC Golf, will let you keep the club for 30 days and return it for a refund, if its extra power doesn't help you cut 6 to 8 strokes off your score (if you average 85 or higher).

To order the Controller Driver, call **1-800-285-3900** or click **www.ngcgolf.com/r** (anytime or day).

Or send your name, address and check (or cc number and exp. date) to NGC Golf **(Dept. OD-20)**, 60 Church St., Yalesville, CT 06492. Ask for the Controller Driver and choose from three shaft models: steel at $149.00, graphite at $179.00 and their top-of-the-line, big-butt TurboTip graphite at $195.00. Add $12.95 s/h. CT add sales tax.

When you buy the driver, the matching 3 and 5-woods are available at a $20.00 discount off the driver's price. Be sure to specify regular or stiff flex, right or left-handed, men's or ladies'.

Oh, yes. If you swing at 120 MPH, carry some extra balls.

MD-8

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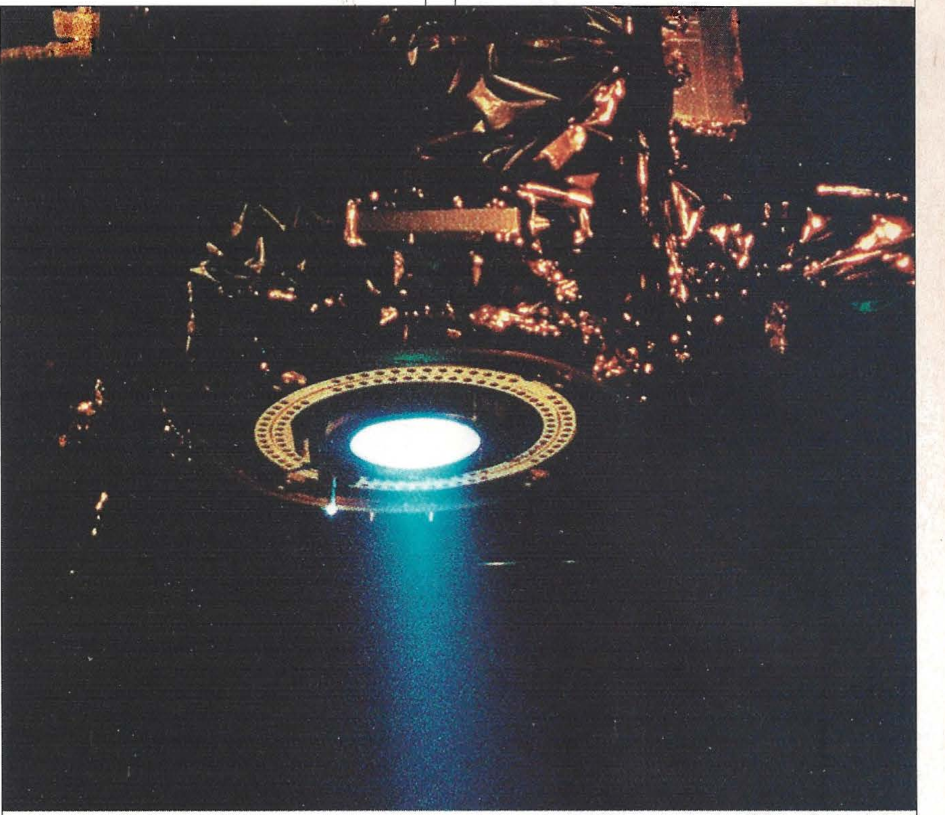
Dept. OD-20

by bob berman

There's more than one way to escape gravity

Faster, Gentler Space Travel



High-speed atom fragments glow blue as they fly from an ion engine during testing. Such engines produce a weak thrust but are roughly 10 times as efficient as chemical rockets.

THIS MONTH'S INCOME TAX DEADLINE MIGHT inspire fantasies of fleeing Earth. But the laws of physics, like the laws of the IRS, are irrevocable. Before you can set up a tax shelter on Mars, there's that little matter of achieving escape velocity.

Getting off our planet requires a textbook speed of 6.96 miles per second. That number applies only if you want to wrench free from Earth's gravity in a one-shot effort, however. If you can wait, a slow, steady thrust can also do the job. Think of Earth as lying at the bottom of a pit. If you drop a rock into the pit, it will have a certain velocity when it hits bottom. One way to get out of the hole is to jump upward at the exact same speed—the escape velocity. Another way out is to climb gradually up the wall of the pit. So long as you generate enough force to keep working your way up the wall, you'll still get out. Heading upward at even one mile per hour, a rocket could work its way out of Earth's gravitational field and travel clear across the universe if its engine fired for a long enough time.

Science fiction writers have long dreamed of building a space elevator, a 22,000-mile-high lift that would permit routine, gradual ascents into orbit. David Smitherman of NASA's Marshall Space Flight Center has even outlined how to create such a device (see the Web site flightprojects.msfc.nasa.gov/fd02_elev.html), although he admits it is at least a century away from feasibility. For now, chemical rockets are the only practical way to ascend the steepest part of our gravitational well. But once you get past Earth's drag-producing atmosphere, a slow escape is both possible and desirable, because a tiny acceleration can produce a huge velocity if maintained long enough. Think the tortoise and the hare.

NASA's *Deep Space 1* spacecraft, which shut down last December 18 after a three-year journey, shows the virtues of the leisurely approach. After a conventional launch, *Deep Space 1* fired up its decidedly unconventional ion engine. Electric current from the probe's solar panels zapped an onboard supply of xenon gas and sent the resulting xenon ions racing out the back at 70,000 miles per hour. The engine generated a feeble thrust, equal to the weight of a couple of sheets of paper on one's palm, but it fired for 16,000 hours. *Deep Space 1* ultimately gained 7,900 mph of extra speed, which enabled it to follow a looping path of discovery past asteroid Braille and Comet Borrelly. NASA is at work on a more powerful Next Generation Ion Engine.

This spring the privately funded Planetary Society will test an even gentler propulsion system, a solar sail. The *Cosmos 1* spacecraft will blast off aboard a Russian chemical rocket. Once in orbit it will deploy eight ultrathin blades that unfurl to form a 100-foot-wide fan. The blades will capture the pressure of the sun's light, providing 1/1000 g of thrust. The force is minuscule, but solar sails use no fuel. As a result, they keep gathering speed without additional resources, steadily ascending the huge slope of the sun's gravity.

Planetary Society director Louis Friedman believes solar sailing is the only practical way to perform the great escape, digging out entirely from the sun's gravitational well for interstellar adventures. The *Cosmos 1* will be a more modest affair, a mere proof-of-concept flight with no specific destination. Still, Friedman is ecstatic: "We feel like the Wright brothers during their first 12 seconds in the air. They, too, went nowhere in particular." And like Orville and Wilbur's biplane, tomorrow's interplanetary sailing ships will produce no head-snapping acceleration—hence, no seat belts required. ☒

The slow approach could even overcome the gravity of a black hole. Contrary to popular belief, a powerful rocket could escape from within a black hole's event horizon. The crew, however, could never go home because an infinite amount of time would have passed in the process.

PHOTOGRAPH COURTESY OF NASA/JPL.

Advertisement

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OTT-LITE® VisionSavers™ are the only lights made that are completely based on a scientific understanding of the eyes. Designed by vision experts, this floor lamp enhances the eye's ability to work tirelessly for hours at computer workstations by replicating the beneficial wavelengths of natural daylight. The results are a new ease in reading, a great reduction in eyestrain, and colors and words that jump off the screen. VisionSaver™ lights give off extremely low heat and are virtually glare-free, resulting in reduced distortion, increased contrast and visual clarity that is significantly greater than typical cool white lamps. The 10,000-hour bulb life uses very low energy while it gives an amazing optical experience.

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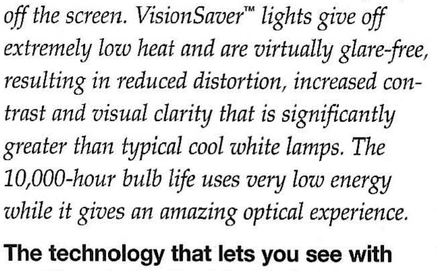

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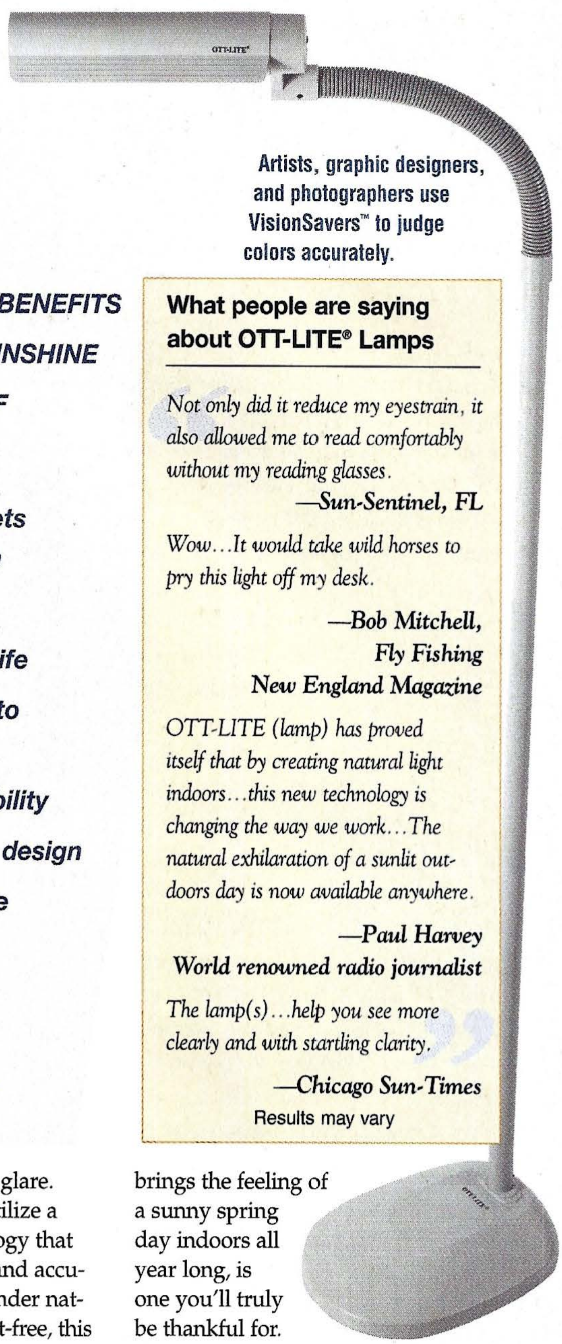

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>
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>
> *Wow…It would take wild horses to pry this light off my desk.*
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> *New England Magazine*
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> *OTT-LITE (lamp) has proved itself that by creating natural light indoors…this new technology is changing the way we work…The natural exhilaration of a sunlit outdoors day is now available anywhere.*
>
> *—Paul Harvey*
> *World renowned radio journalist*
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> *The lamp(s)…help you see more clearly and with startling clarity.*
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The Last Great Mystery

GEORGE LEMAÎTRE MUST HAVE BEEN A FASCINATING FELLOW. A Belgian priest who was also a physicist with a Ph.D. from the Massachusetts Institute of Technology, he proposed in 1927 that the universe began as a single "primeval atom." This atom underwent "radioactive disintegration," Lemaître said, which was his typically poetic way of saying it blew apart. The fragments, he theorized, coalesced into planets and stars. The idea, similar to one advanced by Alexander Friedmann a few years earlier, was generally dismissed.

The skepticism trailed off in later decades as it became clear to astronomers that galaxies are indeed racing apart, as if propelled by some primordial explosion. Astronomer Fred Hoyle coined the flippant term *Big Bang* to describe the universe-by-explosion theory, which he did not accept. He favored the steady-state hypothesis, which held that new matter was being created continually, filling the gaps in an expanding universe. But Hoyle's sarcastic epithet persists, while his pet theory does not. A 1965 paper with the banal title "A Measurement of Excess Antenna Temperature at 4080 Mc/s" by radio astronomers Arno Penzias and Robert Wilson established that there had indeed been a "bang," and its afterglow still permeates the cosmos.

Still, the Big Bang theory remained incomplete. Writer Brad Lemley remembers one of his high school science teachers holding forth on the Big Bang in the early 1970s: "He seemed to think it explained everything. I immediately asked him where all the stuff that went bang came from. He said no one knew, but he also seemed to think the question was unimportant." Lemley thought that the Big Bang theory itself was unimportant. "Who cared about how matter travels?" he says. "To me, it had almost no explanatory power. If you watch a cannonball fly overhead, what does it tell you about how cannonballs are made?"

In the years since, Lemley has come to realize that all roads lead back to Lemaître's alma mater, MIT, and to a professor there named Alan Guth. "His inflation theory dares to address ultimate origins," says Lemley. "After reading about him for at least 15 years, it was a real honor to meet him. He's unassuming, very funny, and willing to take a layman through the physics at a merciful pace."

As Lemley and Guth talked, their conversation led to the implications of inflation theory. If the universe could come from nothing, Lemley asked, what does that mean to us as human beings?

"I think it undermines the belief that we are here for any cosmic purpose," Guth said. "It does not mean that our lives are meaningless. It means we must give meaning to our lives ourselves." That view obviously leaves little room for most of the world's religious teachings.

The next day, Lemley was jogging through the Bowdoin College campus near his home in Topsham, Maine. "I was thinking about Guth's assertion that science can explain the birth of the universe in the context of the laws of physics but has no clue about the origin of those laws." At that moment, Lemley noticed the phrase "Nature's Laws are God's thoughts" etched in granite on the Searles Science Building, built in 1894. "I had passed that building dozens of times and had never seen that before," Lemley says with a smile. "Back then, where those laws came from wasn't a mystery. In 2002 it's the last great mystery."

Most explosions, such as the one triggered here by a dynamite cap, decelerate right after they begin. But the bang that gave birth to our universe expanded at a rate that accelerated exponentially, says cosmologist Alan Guth.

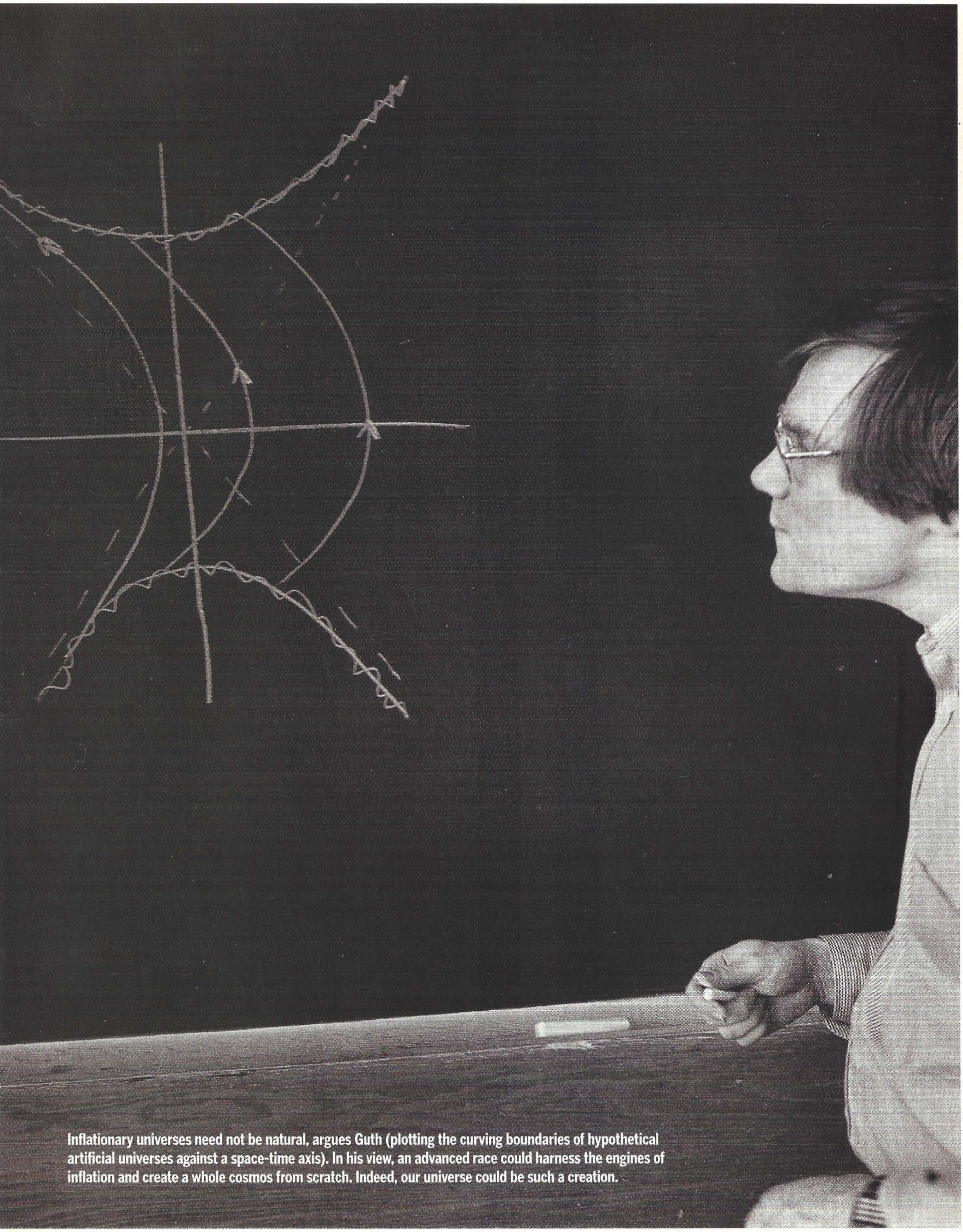
PHOTOGRAPH BY HAROLD EDGERTON

> ‘Most people really want to know where we came from. We have evidence. We no longer have to rely on stories we were told when we were young’

Guth’s Grand Guess

WHERE DID EVERYTHING COME from? Don’t say, “the Big Bang.” To say that everything came from the Big Bang is like saying babies come from maternity wards—true in a narrow sense, but it hardly goes back far enough. Where did the stuff that went “bang” come from? What was it? Why did it bang? ¶ Before Alan Guth came along, cosmologists seldom dared to guess. ¶ The Big Bang theory, based on speculations dating

By Brad Lemley
Photography by Larry Fink



Inflationary universes need not be natural, argues Guth (plotting the curving boundaries of hypothetical artificial universes against a space-time axis). In his view, an advanced race could harness the engines of inflation and create a whole cosmos from scratch. Indeed, our universe could be such a creation.

back to 1922 and confirmed by astronomers in the 1960s, posited that the universe began as a minuscule fireball of extreme density and temperature and that it has been expanding and cooling ever since. But the theory said nothing about what came before or even during the split second when everything went bang. In December 1979 Guth, then 32 and an obscure physicist at the Stanford Linear Accelerator Center, emerged as the first scientist to offer a plausible description of the universe when it was less than one-hundredth of a second old. During an unimaginably explosive period between 10^{-37} second and 10^{-34} second after its birth, Guth said, the universe expanded at a rate that kept doubling before beginning to settle down to the more sedate expansion originally described by the Big Bang theory.

Guth's theory of inflation—the name he coined for this superfast early-universe expansion—has since vanquished every theoretical challenge and grown stronger with each new cosmological finding, including the latest, largest one: that the universe's expansion rate, long thought to be slowing, is actually accelerating. "There's no competition, but that's not for lack of trying," says cosmologist Alexander Vilenkin of Tufts University. "Many people have tried to develop a model that addresses the same problems, and they have failed." Guth's reputation has ascended with the theory: He has gone from an underemployed postdoc to cosmology's leading man. In April of last year, he received the Benjamin Franklin Medal in physics, often a precursor to the Nobel Prize.

Meanwhile, the time has come to contemplate inflation's largest implication, one that seemed overreaching for an unproved theory in 1979 but that now must be faced squarely. The whole universe may be, to use Guth's phrase, "a free lunch." The primordial "stuff" of inflation, he and other cosmologists contend, is very likely a spontaneous creation, a no-strings gift that boiled out of absolutely nowhere by means of an utterly random but nonetheless scientifically possible process. Now that inflation theory is approaching dogma, it is bringing science to the brink of answering one of the largest questions of all: Why is there something rather than nothing?

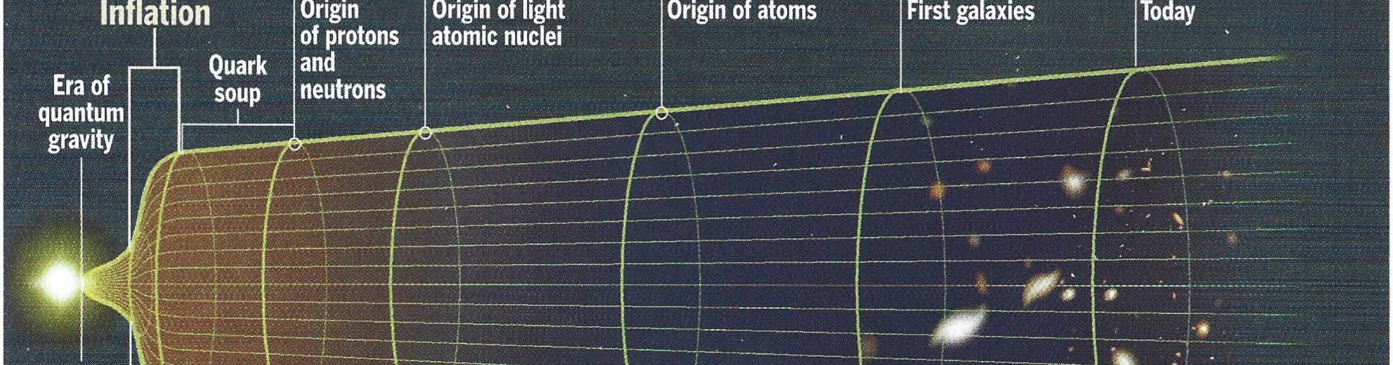
To find out, I walk across campus at the Massachusetts Institute of Technology, where Guth is the V. F. Weisskopf Professor of Physics. His office is in building 6—at aggressively utilitarian MIT, buildings are numbered, not named—at the end of a quarter-mile connector that students call "the infinite hallway." I knock. Guth isn't there. "He's always late," a passing professor says helpfully. Guth's assistant unlocks the door for me.

It looks like something went bang in Guth's office: Even by distracted-genius standards, it is a terrific mess. A pile of 39 empty soda bottles, mostly Diet Pepsi, leans against the wall. The litter includes a half-finished grande coffee, empty computer-parts boxes, and other debris. Covering all the horizontal surfaces is seemingly every paper or book ever written about cosmology, astrophysics, or particle physics. The piles on Guth's desk are higher than his computer monitor. It's a big office by academic standards, maybe 15 by 20 feet, but one must hop between the few clear spaces on the carpet to get anywhere.

And here comes Guth, apologizing for his lateness, hand extended. He is shortish at 5 feet 7 inches and energetic, sort of bouncy. It's easy to believe he was once the champion long jumper at his high school in Highland Park, New Jersey. His

AN INFLATIONARY UNIVERSE

The universe according to Guth began in the era of quantum gravity, a time when all four forces of the universe—gravity, electromagnetism, the strong (nuclear) and weak forces—may have been unified. Energy boiling out of this unstable stew grew during the brief inflationary period at an ever-doubling rate, then decayed into an electron-quark soup as those forces began splitting apart. The soup's fundamental particles combined into ever-more-complex forms as the universe cooled and expanded.



GRAPHIC BY MATT ZANG

neck projects forward at about a 45-degree angle from his shoulders, giving the impression that he is fascinated by everything, which is true. His graying hair covers his ears. He wears gold-rimmed glasses, a blue button-down shirt with no tie, khaki pants, casual brown leather shoes, and one of those nerd watches with a numeric keypad. He talks quickly, with a strong Jersey accent. He is 55, the son of a dry cleaner. He is a family man, with a son in college and a daughter in high school, and he is pleasantly down-to-earth, laughing loudly and often as we discuss the impossible parking situation at MIT.

As Guth talks, he seems naturally to drift back 15 billion years, to the moment when most cosmologists agree the universe began. Soon we are among the nascent stars.

"It's not a coincidence that the Bible starts with Genesis," he says as we leave the building and hustle up Vassar Street, through a chill autumn wind blowing off the Charles River. "Most people really want to know where we came from and where everything around us came from. I like to strongly push the scientific answer. We have evidence. We no longer have to rely on stories we were told when we were young."

We enter a small Italian restaurant on MIT's north side. There is no such thing as a free lunch here. Guth's breaded sole is $10.95—good, he says, and worth the price.

So if eight ounces of fish costs 11 bucks, and if, in a larger sense, nothing in this universe is ever "purchased" without an exchange of energy, how can the whole universe be free?

Start, Guth says, by imagining nothing, a pure vacuum. Be careful. Don't imagine outer space without matter in it. Imagine no space at all and no matter at all. Good luck.

To the average person it might seem obvious that nothing can happen in nothing. But to a quantum physicist, nothing is, in fact, something. Quantum theory holds that probability, not absolutes, rules any physical system. It is impossible, even in principle, to predict the behavior of any single atom; all physicists can do is predict the average properties of a large collection of atoms. Quantum theory also holds that a vacuum, like atoms, is subject to quantum uncertainties. This means that things can materialize out of the vacuum, although they tend to vanish back into it quickly. While this phenomenon has never been observed directly, measurements of the electron's magnetic strength strongly imply that it is real and happening in the vacuum of space even now.

Theoretically, anything—a dog, a house, a planet—can pop into existence by means of this quantum quirk, which physicists call a vacuum fluctuation. Probability, however, dictates that pairs of subatomic particles—one positive, one negative, so that conservation laws are not violated—are by far the most likely creations and that they will last extremely briefly, typically for only 10^{-21} second. The spontaneous, persistent creation of something even as large as a molecule is profoundly unlikely.

Nonetheless, in 1973 an assistant professor at Columbia University named Edward Tryon suggested that the entire universe might have come into existence this way. In a paper titled "Is the Universe a Vacuum Fluctuation?" he stated, "I offer the modest proposal that our Universe is simply one of those things which happen from time to time." Others scoffed at the idea. If a from-nothing, briefly existing molecule is absurdly unlikely, physicists reasoned, a from-nothing, 15-billion-year-old universe is vastly less likely.

WHERE DO RULES COME FROM?

Alan Guth's inflation theory explains the creation of the universe in a way that's compatible with the laws of physics. But where did the laws of physics come from? "One theory is that there are no laws of physics, that there are only properties of matter," Guth says. "According to this view, if there is no matter, then there are no properties."

If that's true then Guth's speculations about how a universe might have started from nothing are absurd. But Guth argues that quantum theory, the best theory yet for describing the physical world, seems to require independent laws. "If you bang two electrons together with enough energy, you produce protons. If there are no independent laws, then all the properties of protons must somehow be 'known' by the electrons. By extension every elementary particle must carry around enough information to produce the entire universe. I find that difficult to believe." Guth adds that quantum theory holds that objects can appear and disappear according to specific laws, and the behavior of an absent object is just as predictable as the behavior of a present one. "If laws are just properties of objects," he says, "how can those laws continue to operate when the object is not really there?" *—B. L.*

So the situation remained for about five years. Then, on November 13, 1978, Guth, while doing postdoctoral research in particle physics at Cornell University, chanced to stroll into a lecture on the Big Bang given by Princeton cosmologist Robert Dicke. At the time, Guth thought the field of cosmology was irritatingly vague, a sandbox of speculative indulgence compared with the mathematically clean world of particle physics. "If the week had been just a bit more hectic, I would have skipped the lecture," he says.

But it wasn't, and he didn't.

Dicke's topic was the flatness problem, one of the Big Bang theory's biggest mysteries. Dicke explained that somehow the universe seems to be extremely "flat," which means matter, velocity, and gravity all balance to put space-time precisely on the dividing line between a "closed" and an "open" geometry. In a closed universe, space-time curves back on itself, such that light beams that start out parallel will actually meet. In an open universe the beams will diverge. The value of omega describes the ratio between the average density of matter in space and what that density would need to be to make the universe perfectly flat. If omega equals one, the universe is flat.

Now back in Guth's office (explaining omega took much longer than the summary above suggests), he hunches forward on his dorm-issue orange couch, his excitement about this subject palpable. "According to classic Big Bang theory, as the universe evolves, the value of omega is always driven away from one," he says. So if the universe starts out with an omega value of less than one, omega gets rapidly smaller as the universe ages. If it starts with omega greater than one, omega gets rapidly larger. The fact that omega is very close to one today—microwave background radiation measurements indicate it is within 10 percent of one—means that, according to classic Big Bang theory, one second after the bang, omega would have had to be between .999999999999999 and 1.000000000000001. But why? "I was intrigued," says Guth. "How could that number start out so finely tuned?"

On December 6, 1979, after more than a full year of mulling over this and other Big Bang mysteries, Guth sat down at his desk and came up with the breakthrough that he called inflation. He realized that omega did not have to be preposterously fine-tuned from the start. An exponentially expanding early universe, which he would come to call the inflationary universe, would drive omega toward one, not away from it, making a flat universe inevitable.

Huh?

All matter plus all gravity in the observable universe equals zero. So the universe could come from nothing because it is, fundamentally, nothing

Return to that primordial vacuum, a boiling stew from which pairs of positive and negative subatomic particles bubble into being for the briefest of instants. Inflationary theory suggests that what erupted was a "false vacuum," a peculiar form of matter predicted to exist by many particle theorists, although the real article has never been observed.

A false vacuum is characterized by a repulsive gravitational field, one so strong it can explode into a universe. Another peculiarity of the false vacuum is that it does not "thin out" during expansion as, say, a gas does—the density of the energy within it remains constant even as it grows. So the false vacuum's expansion, accelerating exponentially as its repulsive force compounded, actually created vast quantities of ever-doubling energy, which decayed into a seething plasma of particles such as electrons, positrons, and neutrinos. As the early universe went along doubling every microsecond, the stuff in it doubled, too—out of nowhere. The electrons, positrons, and neutrinos became a sort of hot soup, which 300,000 years later neutralized to form simple atoms. The simple atoms, like hydrogen, helium, and lithium, were ripped apart and crushed together to form more complex, heavier atoms inside stars. Exploded into space by supernovas, they became the matter we see—and are—today.

The initial bit of false vacuum required by Guth's calculations turned out to be mind-bendingly small: A patch one-billionth the size of a proton would do. And the required period of exponential growth was very short. In perhaps just 10^{-34} second, he suggested, the universe expanded by 25 orders of magnitude, to roughly the size of a marble, an increase equivalent to a pea growing to the size of the Milky Way.

The inflationary process, Guth discovered, would push omega toward one with incredible swiftness. The reason is best expressed by analogy. The universe appears to be virtually flat for the same reason that Earth's surface appears to be virtually flat to a person standing on that surface. The very fabric of space becomes relatively "stretched" so that in as few as 100 doublings in size, its curvature is effectively canceled.

And what about the conservation of energy? According to Einstein's theory of relativity, the energy of a gravitational field is negative. The energy of matter, however, is positive. So the entire universe-creation scenario could unfold without breaking conservation-of-energy laws. The positive energy of all matter in the universe could be precisely counterbalanced by the negative energy of all the gravity in the universe.

This also is more than theory. Observations are consistent with the idea, and calculations totaling up all the matter and all the gravity in the observable universe indicate that the two values seem to precisely counterbalance. All matter plus all gravity equals zero. So the universe could come from nothing because it is, fundamentally, nothing.

"It is rather fantastic to realize that the laws of physics can describe how everything was created in a random quantum fluctuation out of nothing, and how over the course of 15 billion years, matter could organize in such complex ways that we have human beings sitting here, talking, doing things intentionally," says Guth, leaning, if possible, even farther forward.

Three weeks later I attend a lecture Guth gives to the New York Academy of Sciences. It's an august gathering, sold-out, and Guth handles questions with aplomb, even an off-the-wall query about "negative consciousness waves" stemming from the September 11 terrorist attacks (Guth suggests that rational thought, such as what cosmology brings to bear on the origin of the universe, could make the world a more peaceful place).

But how do we know if any of this is true?

"There really are tests," Guth says. Readings from the Cosmic Background Explorer satellite, launched in 1989, show that the temperature of the radiation that pervades the universe is astoundingly uniform. Standard Big Bang cosmology theory without inflation offers no explanation. Some mechanism would have to transmit energy and information at about 100 times the speed of light for these vastly distant parts of the background radiation to "know" and reflect one

Some cosmologists are as remote as their subject matter, but not Guth, who eagerly strides to the podium for a public lecture at MIT. "It's fun to see what kind of impact these ideas have on people who have not heard them," he says. "It rejuvenates my excitement."

another's temperature. Inflation, expanding at faster-than-light speed, is the only known way such uniformity could be spread so widely. (Incidentally, such expansion does not violate the cosmic speed limit. Einstein correctly asserted that nothing in the universe could exceed light's speed, but even as the cosmos grew at faster-than-light speeds, no particle within it could ever win a race with a beam of light.)

Inflation theory also predicts what are called density perturbations—small ripples in this uniformity that become seeds for galaxy formation. The galaxies we observe today are just what inflation theory suggests should have been created. "The theories we have developed so far seem to be working shockingly well," Guth says.

Still, cosmologists busily fiddle. Roughly 50 forms of inflation have been proposed, named, and studied, including double, triple, and hybrid inflation, tilted hybrid inflation, hyperextended inflation, and inflation that is "warm," "soft," "tepid," and "natural." In 1997 Guth tallied 3,000 published papers devoted to the subject; he has since stopped counting. Guth in particular credits cosmologists, including Stanford's Andrei Linde and Princeton's Paul Steinhardt, with refining the theory, but each variation preserves the essential elements of Guth's original brainstorm: Some state plays the role of the false vacuum and its repulsive gravity, and some decay of that state leads to the formation of matter. The details, Guth believes, will tumble out of university labs, particle accelerators, and deep-space satellite readings for decades, if not centuries.

The latest wrinkle is that observations by two teams of astronomers in 1998 show that the rate of cosmic expansion is accelerating, not slowing as had previously been thought. If these observations are right, Guth says, they offer proof that gravity can act repulsively. In fact, the same type of repulsive force that originally powered inflation probably drives the universe's current acceleration. Since energy and mass are equivalent, this repulsive energy must also exert gravity, and if there were enough of it, it would preserve the original mass-gravity balance required to make the universe flat. Inflation theory triumphs again.

Guth is pursuing this and other cosmic investigations, but I frankly wonder how much headway he can make. As we speak in his office, constant phone calls, urgent e-mails, and bureaucratic folderol assail the poor guy. A confused freshman raps on the door, seeking approval for a transfer. A fellow physics professor returns Guth's call: The "right" answer in the freshman physics quiz, Guth contends, isn't right enough, and they debate this for a while. It's odd. If Alan Guth is the man who answered the central question of human existence—the origin of the universe—neither he nor those around him seem terribly awed by the fact.

Or perhaps that shouldn't be surprising. Human beings have evolved to survive in this universe, not necessarily to be able to understand it. A false vacuum, jittering from nothing into actuality and then erupting into a universe—or according to some newer variants of inflationary theory, an infinity of universes—is the kind of knowledge that tends to slide off the brain. Guth remains obscure among the public at large because the theory itself remains rather inaccessible. Large sections of his 1997 book, *The Inflationary Universe,* are very heavy sledding, despite Guth's earnest efforts to make the underlying physics clear.

Guth admits that some aspects of his work are challenging even for him. In one of the most charming sections of the book, he describes his first attempt as a particle physicist to explain inflation to a group of astrophysicists. "I understood very little of what they were saying, so I had no idea why we were disagreeing," he wrote.

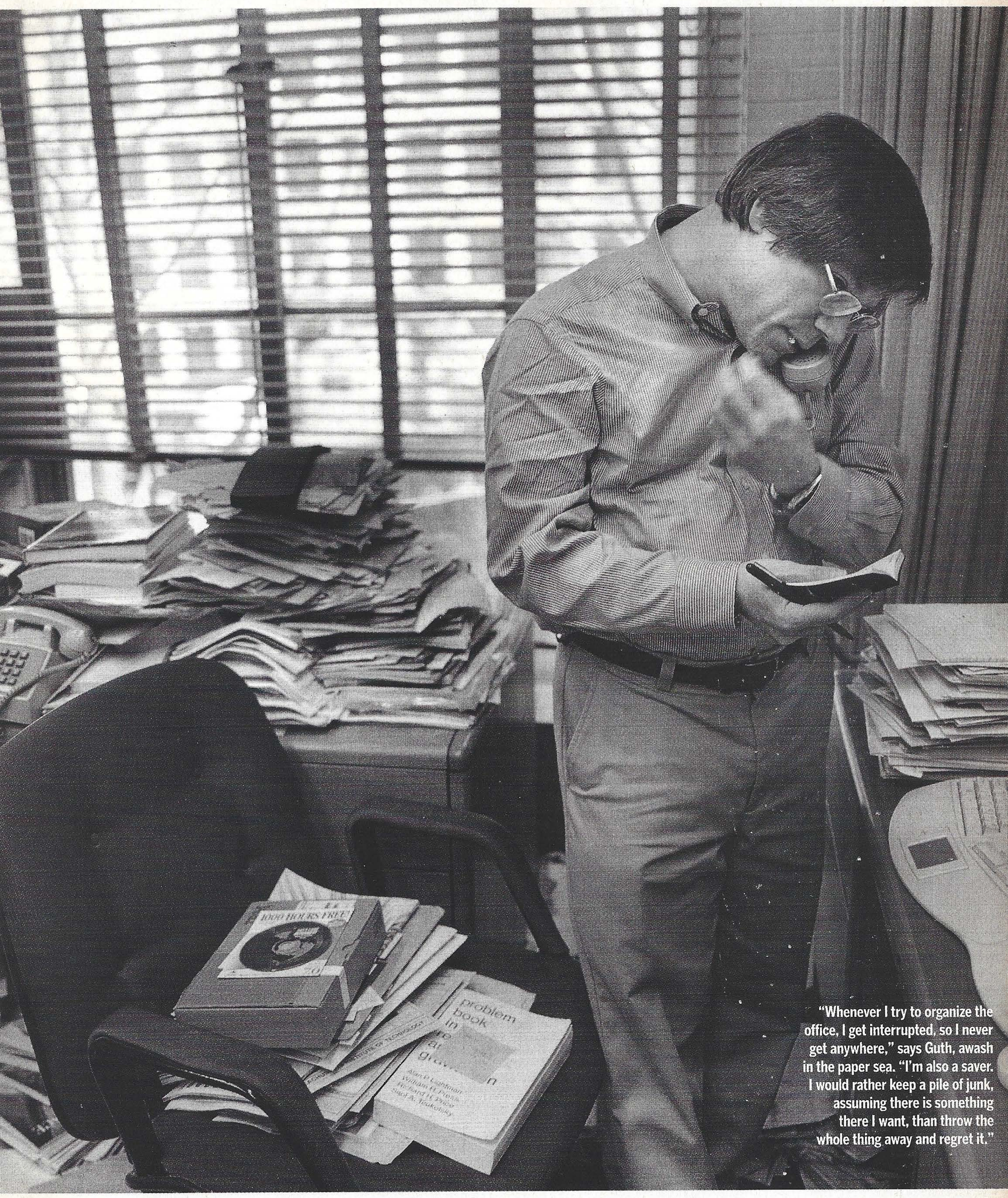
So let's be clear. Is Guth saying that cosmology can crack the ultimate mystery? That creation can be just another physical process that science has rendered prosaic, like the discovery that germs cause disease or Earth circles the sun?

Guth smiles and puts his fingertips together.

"I like to be careful how I put that," he says. "The way I like to say it is that we are approaching a scenario for the creation of the universe that is compatible with the laws of physics. That raises the question: 'Where do the laws of physics come from?' " He pauses. "We are a long way from being able to answer that one." ☒

INFINITE INFLATING UNIVERSES

So far, what inflation theory predicts, the observable universe has reflected. But cosmologists Andrei Linde, Alexander Vilenkin, and others have run with inflation's premises to step beyond the bounds of what we can see or measure. They speculate that the decay of the false vacuum—which, according to the inflation theory, created the matter of our universe—does not happen all at once. While some regions decay into universes, other regions keep expanding and creating other universes. Residual false vacuum from the creation of those universes creates still others, indefinitely. Linde and Vilenkin call this "the eternally existing, self-reproducing inflationary universe." Guth contends that this scenario is not only possible, it seems like a sure thing. "If a biologist discovered a bacterium that belonged to no known species, she would presumably invent a new species in which to classify it," Guth wrote in his 1997 book, *The Inflationary Universe*. "However, even though only a single specimen of the new species had been found, she would undoubtedly assume that it was the offspring of a bacterial parent cell." Guth predicts that "any cosmological theory that does not lead to the eternal reproduction of universes will be considered as unimaginable as a species of bacteria that cannot reproduce." *—B. L.*



"Whenever I try to organize the office, I get interrupted, so I never get anywhere," says Guth, awash in the paper sea. "I'm also a saver. I would rather keep a pile of junk, assuming there is something there I want, than throw the whole thing away and regret it."

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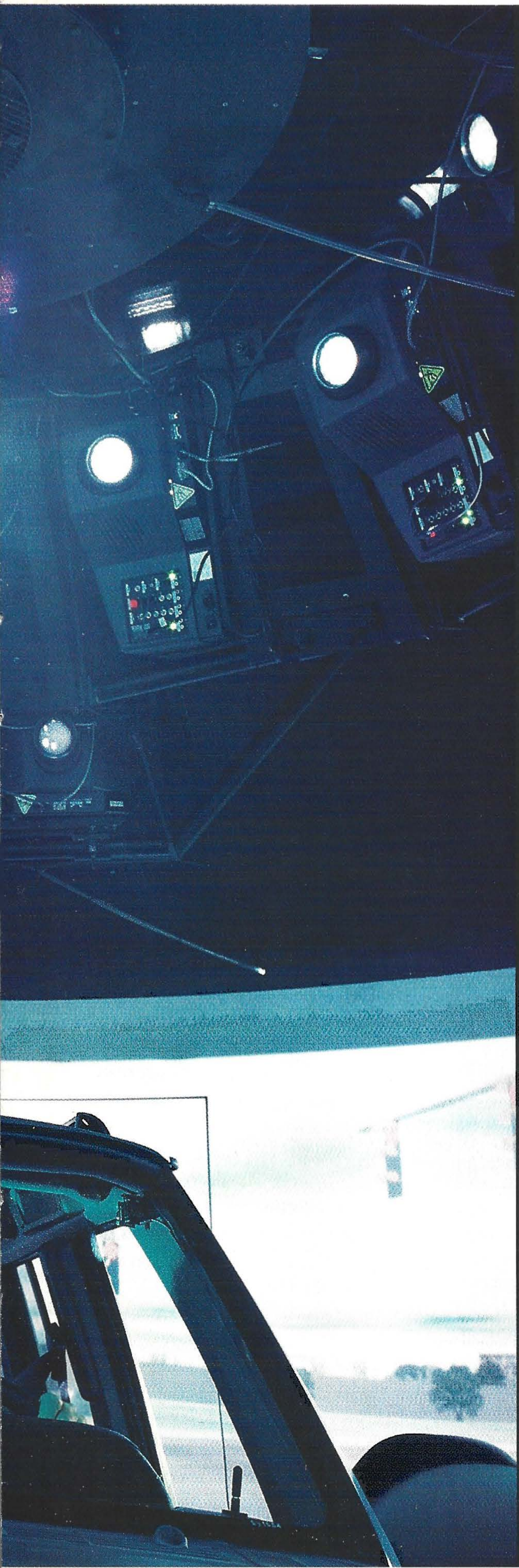
Seated at the wheel of the most advanced driving simulator in the world, this woman can't see the 15 projectors overhead that create a virtual world so real she will forget her car is on the road to nowhere.



HIGH TECHNOLOGY

Four hours' sleep last night, a glass of wine at the office party, an antihistamine for a stuffy nose, and here comes a car full of teens, head-on, drifting into your lane.

(Be glad you're in the National Driving Simulator.)

BY SAM HOOPER SAMUELS

PHOTOGRAPHY BY KATHARINA BOSSE

THE DRUNKEN. THE DRUGGED. THE DROWSY. Ginger Watson puts them behind the wheel of her Chevy Malibu every day and then sets them loose in traffic, just hoping that they'll get into a really messy crack-up.

"You have to see people falling asleep behind the wheel of a car," Watson says gleefully.

Fortunately for those drivers, the danger is purely virtual. That Malibu isn't exactly a real car. It's a Chevy, all right, with real seats and real controls, but instead of wheels it sports hydraulic actuators that do a convincing imitation of the rumble of tires on a road. Flip up the hood, and instead of an engine there's a tangle of cables and computers. Step outside the vehicle, and the landscape fades away if viewed from the wrong angle. This demolition derby car that easily goes from 0 to 60 does it in a huge simulator. Here, Watson, director of the Human Factors Laboratory at the National Advanced Driving Simulator, can test any driver in the most awful scenario imaginable and do it over and over again.

Driving simulators have been used for years to research roadway designs, train drivers, and test consumer acceptance of new cars. The range of sophistication runs from primitive simulators with a PC screen and a joystick to those with realistic car controls and road sounds. The DaimlerChrysler simulator in Berlin—until recently the best in the world—is mounted on a track about 20 feet long and adds motion to a virtual experience: Hit its brakes hard, and the cab shoots backward, throwing the driver forward into the steering wheel.

When the National Advanced Driving Simulator became operational in January, it put the German machine in the shade. For the first time, a driver in a simulator finds the world around him so believable he forgets that the car swerving into his lane isn't real. Believability wasn't cheap—most of the $80 million it cost to develop and build the simulator at the University of Iowa's Coralville research facility came from the National Highway Traffic Safety Administration.

Still, the price can seem low compared with the cost of losing about five lives every hour in highway-related accidents. Keith Brewer, director of the Office of Human Centered Research at the National Highway Traffic Safety Administration, says that traffic accidents cost us more than $150 billion a year.

THE IOWA SIMULATOR IS MOUNTED ON A PAIR OF LONG BEAMS THAT work at right angles to each other. One beam moves forward and backward, the other side to side, allowing movement within 4,356 square feet. Because the simulator's dome can move freely and quickly, it can help create a sense of pitch. If a driver hits the brakes, the Chevy will not only shoot backward and lower its nose, but the image on the giant screen around it will rise slightly. The machine can also throw a driver sideways or even transform the world into a dizzying merry-go-round during a skid.

Watson says true feeling of movement makes all the difference: "If that feeling you get back from the car is like the real world, your performance will match the real world very closely. If it doesn't, you will do some odd things." Instead of braking hard when confronted by a sudden hazard, for example, drivers in fixed-bay simulators tend to apply and release the brakes several times before going into a hard-braking maneuver. "You feel like you're not stopping," Watson says, "so you make adjustments you wouldn't make in a panic situation."

There's another problem with fixed-bay simulators: They make people sick. When the visual cues and the motion cues that a simulator feeds to a driver don't match up, the driver may develop so-called sim sickness, which often starts with sighing and a feeling of warmth, then progresses through headache and eyestrain to full-blown nausea.

The Iowa simulator keeps cues in sync with what engineers call nine degrees of freedom. The DaimlerChrysler simulator has only seven. Technically, any object in three-dimensional space has six degrees of freedom. The first three include moving forward and back, side to side, and up and down. Moving diagonally doesn't count as another degree of freedom because it's a combination of the first three. The second three freedoms include rotating forward and backward on an axis, called pitch; rotating like an airplane tipping its wings, called roll; and rotating sideways as if on a turntable, called yaw.

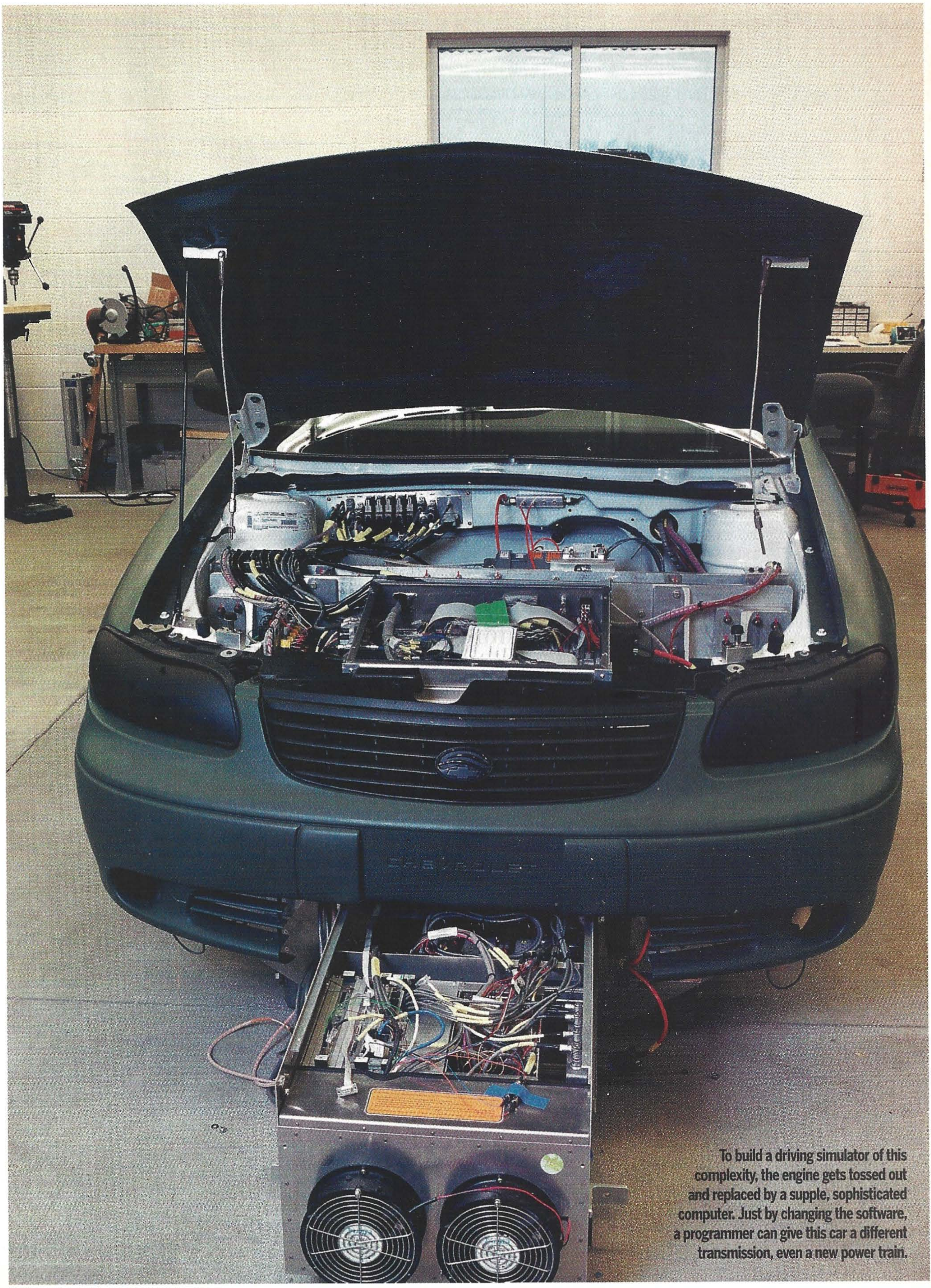
'IF THAT FEELING YOU GET BACK FROM THE CAR IS LIKE THE REAL WORLD, YOUR PERFORMANCE IS GOING TO MATCH THE REAL WORLD VERY CLOSELY. IF IT DOESN'T, YOU WILL DO SOME ODD THINGS'

The Iowa system picks up an additional three degrees of freedom because the car can also move within a huge 66-by-66-foot square. If a simulator has two mechanisms to achieve a particular degree of freedom, engineers say the machine has an additional degree. In the case of the National Advanced Driving Simulator, for example, there's more than one way to move forward and backward. The six legs the car is mounted on can move it short distances, and the 66-by-66-foot motion base can move it longer distances.

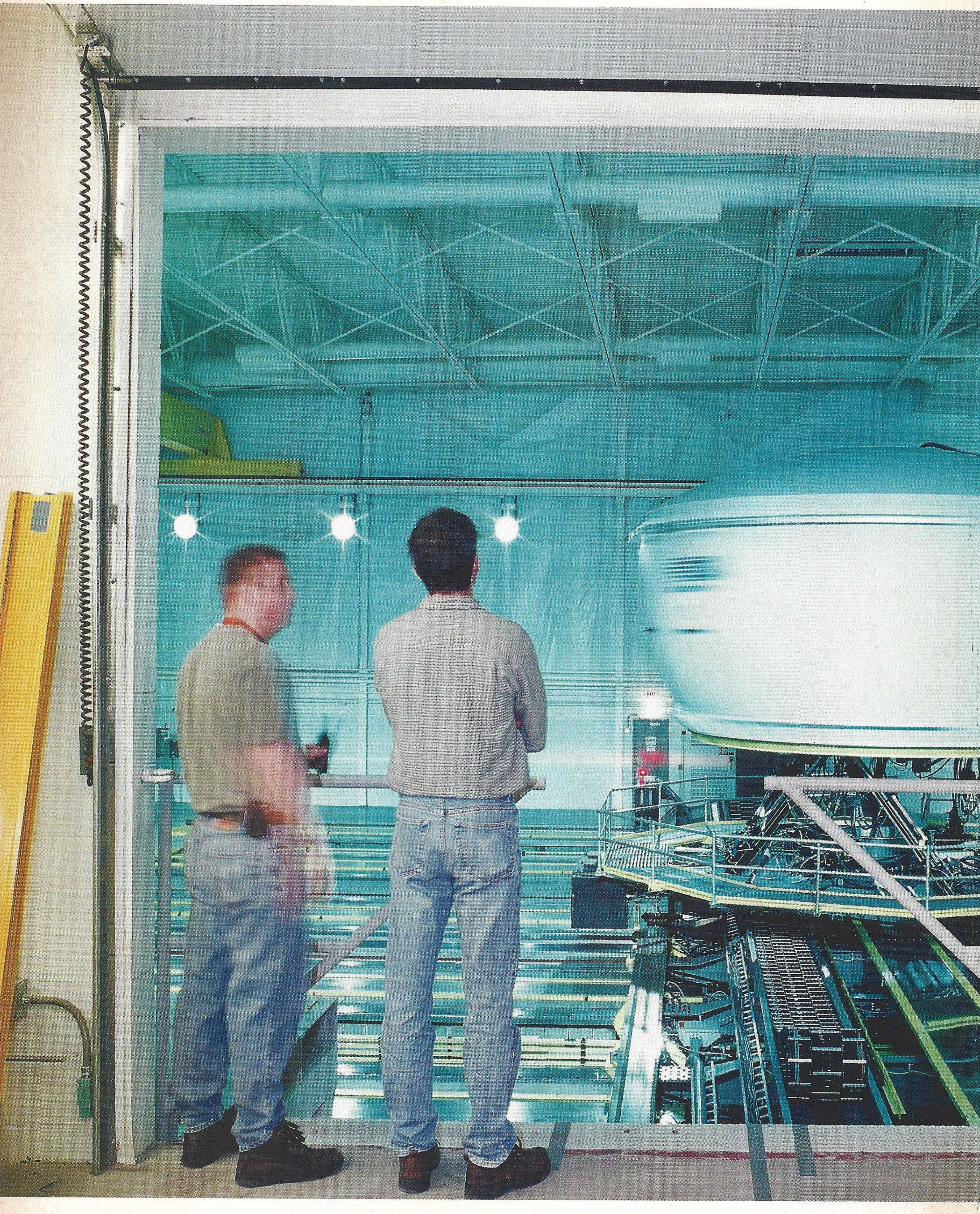
As important as motion is to simulating the experience of driving, Watson says roughly 90 percent of driving is visual. The DaimlerChrysler machine sports a 180-degree field of view. The Iowa simulator surrounds the driver with a full 360-degree view. A ring of video projectors suspended from the roof casts high-resolution images on the inside surface of the dome, creating a sense of immersion. These visuals refresh at a rate of 60 frames per second, more than double the 24 frames per second of a conventional motion-picture projector. The inside surface of the dome, covered with a highly reflective coating, is designed to mirror almost all its light at the driver's eyes to achieve real-world brightness. "We call it the half-a-million-dollar paint job," says Yiannis Papelis, the facility's chief technical officer.

The details of the simulator's rich visual world are lodged in software pieces called tiles that represent highways, residential neighborhoods, commercial and industrial zones, rural scenes, even a winding mountain road 15 miles long. Using a program called a tile mosaic tool, designers create complex environments, such as a town with suburbs leading out into open country. The tiles can be used repeatedly with slight variations.

Technicians can also choose the time of day and weather, combining a visual scene with mechanics that change the car's



To build a driving simulator of this complexity, the engine gets tossed out and replaced by a supple, sophisticated computer. Just by changing the software, a programmer can give this car a different transmission, even a new power train.



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NADS

Tad Gates (left), simulator operations manager, and Jeff Dolan, senior hardware engineer, work to perfect the dome and the car inside it every day. They know some test drivers will be tempted to push the car beyond its limits, and so, Dolan says, "we do a fair amount of that ourselves to learn the limitations of the machine."

performance. For example, in a rainy nighttime scene, the car may drive as though the road is slippery.

One of the most difficult elements to engineer is randomness. "The real world is never regular," Papelis says. "Not everybody will stop at a stop sign exactly the same." The problem is that when researchers run the same test repeatedly with different subjects, or even with the same person under different conditions, the two tests must be nearly identical to yield comparable results. Yet to be both believable and reliable, the simulator must supply chaos as well as order. To solve this dilemma, Papelis and his team devised software programs called run-time coordinators, which he describes as "intelligent agents that are running on the computer while the simulation is running." Coordinators are able to decide when the driving environment may be random and when it needs to be controlled. For instance, an experiment may call for a driver to react to a bus pulling abruptly into his lane. The coordinator might allow the participant to drive around in randomly generated traffic for 15 minutes. Then when the car approaches the important intersection, the coordinator takes control. Red lights turn green; unimportant actors move unobtrusively to the sidelines; the crucial bus makes its entrance. In this way, drivers can drive through the same scenario repeatedly without realizing that they are doing so because only key elements remain the same. The rest of the time, they feel as though they're driving through a very uncertain, and therefore very real, world.

LESS SOPHISTICATED SIMULATORS HAVE ALREADY YIELDED A LOT OF information about drivers. Recent studies, for example, found that drivers under the influence of first-generation antihistamines—widely available without prescription—can be more dangerous than drivers under the influence of alcohol. Drunk drivers have poor reaction times but are often capable of following along in traffic. Drivers using antihistamines show the same lack of control but also tend to nod off at the wheel.

Researchers believe the Iowa simulator can further their understanding of drunk driving as well. States have been limited to setting illegal blood-alcohol levels based on statistics about drivers who have already been in accidents. Using the Iowa simulator, scientists will be able to observe drunk drivers in action, record their pulse rates, measure how far they stray from their lanes, and find out how drunk is too drunk to drive.

Other examples of how the simulator might be used are almost endless. Studies are already under way to measure how safe it is to drive and use a cell phone at the same time. And both manufacturers and academics will be allowed to use the facility. Manufacturers already have plans to plug new-car specs into the device to see just how safe a prototype is before it's built.

The answers to some questions will eventually require an even better simulator. Watson, for example, envisions an MRI-like brain scanner "mounted in the roof of a car to look at what happens when people are driving, which will enable us to know what they are really thinking and what area of the brain they are using in different conditions. That's way out there," she says, but in an age when computing ability doubles every two years or so, who can predict how soon a certain building in Coralville will be better used as a gym? ☒

talking plants

Plants have more than thorns and thistles to protect themselves—they can cry for help

BY SHARMAN APT RUSSELL PHOTOGRAPHY BY MAX AGUILERA-HELLWEG

IAN BALDWIN WORKS IN A LAB ANYONE COULD LOVE: A LARGE blackened burn area high on a steep slope in the Great Basin Desert of southwestern Utah. Here a distant mountain range shimmers blue and lavender, the nearer craggy cliffs of Veyo Ridge hover in red, and the curves of the desert hills are dotted green by Joshua trees and scrub. Baldwin, a biologist and the director of the Molecular Ecology Department at the Max Planck Institute for Chemical Ecology in Jena, Germany, has stationed his equipment here to launch a new study of how plants defend themselves—a question he has pursued for 20 years. ¶ He and his colleagues are using chemical sensors to investigate plant communications: cries for help, invitations, even warnings, each in the form of odor molecules that float past human noses unnoticed. The harder biologists look for these signals, the more they find. They have already discovered that plants can send chemical cues to repel insect enemies, as well as signals that attract allies—other insects that are pleased to eat the insects eating the plant. But that is only the start of a more complex scenario, for Baldwin and others have also

Opposite: Ian Baldwin and his team set up equipment in the Utah desert to monitor wild tobacco's chemical defenses against enemies like caterpillars (shown below). Baldwin had not expected to detect any effects. "The fact that it worked was an amazing surprise," he says. "I turned from a skeptic to a believer. The nice thing about research is you can prove yourself wrong."

found that nearby plants can listen in to this conversation and gear up their own defenses.

"Eventually, we will use the information we get here to breed agricultural crops that call out to their insect allies more loudly and more consistently," says Baldwin.

The scorched area they're studying was struck by lightning a year ago, clearing the hillside of juniper and sagebrush. Smoke from the fire triggered the germination of wild tobacco seeds dormant in the soil, yielding a field of *Nicotiana attenuata.* Baldwin's team has tagged many of them for experiments, using Popsicle sticks and small flags made of red nylon. Chatting in German and English, Baldwin's colleagues look expectantly for golden eagles. The day is hot, the air scented with desert cliff rose.

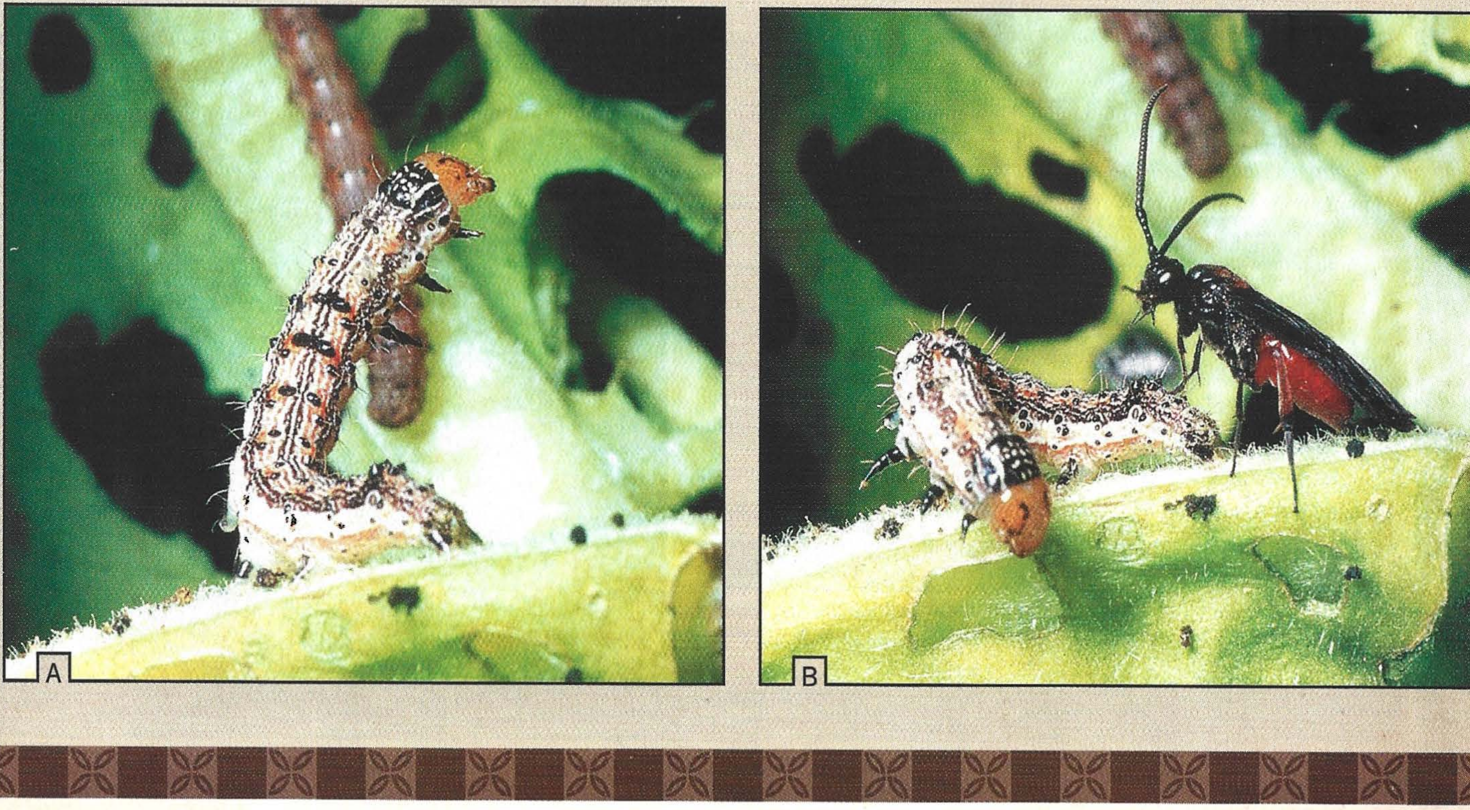
Tobacco plants are good subjects because they must be especially agile with their defenses if they are to survive. The seeds can lie dormant for over a century between fires, so the plants may face new enemies once they start growing. Moreover, when the seed germinates, it has only one season to flower and reproduce—and avoid being demolished by insects. "It has to optimize its growth, and it has to strategize against herbivores, always watching the bottom line, which is setting seed," says Baldwin. "These plants have an amazing plasticity. They have to respond to the environment, which is always changing. A number of insect species feed on *N. attenuata,* and it is a different mix of species every year."

Successful seedlings must fend off the caterpillars of certain hawkmoths, not to mention leaf bugs, flea beetles, and tiny mirids. Baldwin and Andre Kessler, a graduate student, have helped nature along by bringing with them laboratory-raised caterpillars. They place a hungry caterpillar on several of the plants. Over the next few days, they return with a solar-powered gas chromatograph to detect molecules emitted by the damaged leaves. They also check to see what nearby control plants, sans caterpillars, are doing.

Scientists have known for some time that plants can activate powerful defense systems, much as humans churn out antibodies to defend against pathogens. When a caterpillar bites into a leaf, for example, the plant recognizes compounds in the insect's saliva and initiates a chemical defense. Many plants produce toxins (nicotine works well) to kill the insect, as well as compounds that slow down or stop the invader's ability to digest the plant.

Should that fail, there is a second line of defense. A tobacco plant under attack also releases a blend of airborne chemical repellents. In one recent study, Baldwin and Kessler were able to identify, isolate, and test some of these emissions. When they combined the specific chemicals into a paste and smeared it on the stems of plants that had not yet been attacked, hawkmoths avoided laying eggs on them.

Baldwin wanted to find out whether tobacco plants had even more weapons in their arsenal. So he designed an experiment to see if they could summon help. First, he treated the plants with a range of synthetic pastes. Sometimes the paste contained only one of the volatile compounds they had earlier identified, and sometimes it contained a blend of these compounds. Next, they glued the eggs of hawkmoth caterpillars to the underside of the treated plant's leaves. Then they kept an eye out for *Geo-*



A series of photographs taken in the lab of entomologist Consuelo De Moraes shows how some plants can summon help when they're attacked. (A) The common crop pest *Heliothis virescens* feeds on a tobacco plant. Chemicals in the caterpillar's saliva prompt the plant to release airborne chemical cues. (B) Those signals summon *Cardiochiles nigriceps,* a parasitic wasp that prefers to lay its eggs in *H. virescens.* (C) The wasp wrestles with the caterpillar, ultimately laying a single egg inside it. When the egg hatches, the larva feeds on the caterpillar, eventually killing it. De Moraes's work has shown that the cues are tailored to attract specific insect allies.

PHOTOGRAPHS COURTESY OF ANDREI SOURAKOV AND CONSUELO M. DE MORAES.

'Today, the scientific community agrees that plants talking to their bodyguards is likely to be a characteristic of most, if not all, plant species'

coris pallens, an insect that likes to eat the eggs. Sure enough, three of the compounds emitted by tobacco plants seemed to attract *G. pallens,* a small, fast, and rapacious predator.

"By releasing certain volatiles, a plant can reduce the number of herbivores attacking it by as much as 90 percent," Kessler says with admiration. "Chemical signaling is normal. This kind of communication is normal. I think it is probably going on all the time, all around us."

Baldwin explains how he thinks the signals developed. "You're wounded. You emit something. An insect responds. A mutualism evolves."

BALDWIN IS ONE OF THE FIRST IN HIS FIELD TO INVESTIGATE CHEMICAL signaling among plants in the wild. Previous experiments had focused on signaling in domesticated crops, and all that work was done in controlled environments, in bell jars and labs and greenhouses with altered atmospheres. Wind tunnels were supposed to mimic one of nature's wilder forces.

Some of the most complex studies came out of these controlled environments. In 1988 Marcel Dicke and his colleagues at Wageningen University in the Netherlands offered evidence that plants under insect attack could enlist help from the enemies of their enemies. Dicke found that when spider mites attack lima bean plants, the plants release a chemical SOS that attracts another mite that preys on the spider mite. Mechanically damaged plants do not produce the cues; most likely, only elicitors in the saliva of the insect can trigger the plant to produce the right molecules. "Today," Dicke says, "the scientific community agrees that plants talking to their bodyguards is likely to be a characteristic of most, if not all, plant species." Even the gingko—a species that has been around for 150 million years—can communicate chemically with insects, he adds.

For example, when caterpillars feed on corn, tobacco, and cotton, the beleaguered plants produce airborne chemicals that attract parasitic wasps. The chemical cries for help are quite specific, attracting only the wasps that lay their eggs in the type of caterpillar infesting the plant. "Plants are not just saying, 'Yes, I am damaged,' they are also saying specifically who is damaging them. It is such an intricate and fabulous system," says Consuelo De Moraes, an assistant professor of entomology at Pennsylvania State University.

Plants can also time the release of different signals to have different effects. Parasitic wasps hunt during the day, for example, so that's when infested plants release their SOS. Plants time the emissions of repellents as well. In studies of commercial tobacco, De Moraes and her colleagues found that caterpillar-infested plants release a chemical blend at night that seems to discourage nocturnal moths from laying eggs that in turn would produce tobacco-devouring caterpillars.

The idea that plants can signal insects has long made sense to scientists. But the concept that plants can communicate with other plants has not, as Baldwin learned back in the early 1980s while still an undergraduate at Dartmouth College. He was studying trees with biologist Jack Schultz, and in 1983 they published a controversial hypothesis: Airborne chemical cues from damaged maple and poplar trees seemed to boost the chemical defenses of undamaged trees nearby. *The Secret Life of Plants,* a best-seller in the 1970s, had sold the public on the notion of talking to philodendrons, and now it seemed the philodendrons were talking back. Inter-tree communication! Maples whispering to other maples! Reports in the popular press about Baldwin and Schultz's work appeared first in the *National Inquirer* and later in both *People* and *The New York Times.* Scientists were dismissive, and the resulting furor made it difficult for Baldwin and Schultz to get further studies funded.

Time, persistence, and good science has changed attitudes. Several months ago Dicke helped produce a special issue of the journal *Biochemical Systematics and Ecology* filled with papers on plant-to-plant communication. Researchers now find it reasonable that plants can pick up on—and use—each other's signals. "If plants talk to their bodyguards," says Dicke, "then why would their neighbors not take advantage of that and eavesdrop on the message? The topic of plant-to-plant communication is back on the agenda, and the evidence is accumulating."

Dicke and his colleagues have found that mere exposure to airborne emissions from mite-infested cotton and lima beans

'We have been slow to appreciate that plants do many similar or even identical things when responding to insects that they do when responding to pathogens'

will prompt undamaged plants to release signals that summon an enemy of the infesting mite. Over the last 19 years, in various experiments, researchers say they've caught willow, poplar, alder, and birch trees listening to their own kind and barley seedlings listening to other barley seedlings. In each case, damaged plants, whether eaten by caterpillars, infected by fungus or powdery mildew, infested by spider mites, or even clipped mechanically, sent out chemicals that seemed to jump-start the defenses of undamaged plants nearby. Researchers are also testing soil to see if plants release chemical warnings from their root systems.

Even unrelated plants can pick up on chemical alarms. Studies by Baldwin's team and others have shown, for example, that sagebrush normally emit an airborne version of a defensive signal; cut or wounded sagebrush release more than six times as much of the signal as unharmed sagebrush. Tobacco plants transplanted downwind of the wounded sage suffer less insect damage than tobacco plants transplanted downwind of unwounded sage. Other studies have found that cucumbers seem to respond to the signals of injured lima beans.

"We have been slow to appreciate," says Jack Schultz, now a professor of entomology at Penn State, "that plants do many similar or even identical things when responding to insects that they do when responding to pathogens. A completely parallel story may emerge here in the way plants detect nearby infection and gear up for it."

Still, biologists who study plant signaling are careful not to overstate their results. Schultz, who continues to collaborate with researchers like Consuelo De Moraes, believes that Baldwin's pioneering research outside the laboratory brings us much closer to understanding how plants communicate chemically in a natural ecosystem. But Schultz cautions that more experiments must be done. Biologists haven't yet documented the signal traveling from plant A to plant B, and many variables can influence a plant's response: wind, drought, light, touch, and disease. "There are a lot of interacting factors to be sorted out," he says.

Dicke adds that individual plants respond differently to insect attack. How they respond may depend on the availability of nutrients and whether the plant would rather invest in growth or defense. Or it may depend on the age of the plant and whether it would rather focus on growth or reproduction. Or it may depend on the previous experience of the plant, which might strengthen its response.

"Showing how things work outdoors is crucial," Schultz says, "but it is not at all easy."

Information from the wild, where few researchers have ventured, could lead to truly revolutionary changes in agriculture. Farmers now rely on heavy pesticide use because domestic plants, which have been bred for high yield, have often lost their native chemical defenses and cannot call out for help. A wild cotton plant, for example, can emit up to 10 times more airborne emissions that summon parasitic wasps to attack infesting caterpillars than a hybrid can.

"Crop plants have been selected for improved yield and high-quality yield and for resistance to pests and disease," explains Dicke, "but never for compatibility with biological control. The latter is essential for the development of durable and environmentally benign pest control. In nature, plants are exposed not only to herbivores but also to a multitude of those herbivores' natural enemies. In agriculture the number of natural enemies is usually reduced because agricultural systems are usually much more simple. Those natural enemies that are there—or that we introduce there—should be cherished, and their labor conditions should be optimized so as to take full advantage of their services."

Researchers in developing countries are already using knowledge of plant communications to devise arrangements that push pests away from one crop and pull them toward another target. In East Africa, where stem-borer caterpillars devour fields of maize and sorghum, planting molasses grass in the fields pushes pests away. The molasses grass emits airborne chemicals that repel stem borers and attract the caterpillar's predator, a parasitic wasp. At the same time, plants that stem borers like to eat can be grown around the fields, pulling the pest from the main crop. To some extent this mimics what good gardeners have always known intuitively: Certain plants seem to do well together.

Baldwin and Kessler hope their research indicates nature-based pest control might be easily adapted to many plant varieties. The wild tobacco plant, they've found, emits an array of common compounds that attract an all-purpose insect ally whose tastes range from caterpillar eggs to leaf bugs and mirids.

"The natural system may not be so fine-tuned or so specialized that we can't reproduce it fairly easily," Baldwin says. "We don't have to get it perfectly."

IT'S NEARING DUSK, AND BALDWIN AND KESSLER ARE SETTING UP THEIR equipment. Silhouetted against blackened brush, Baldwin pauses to listen to a bird. "Sounds like an oriole," he says.

"No," says Kessler, "a mockingbird imitating an oriole."

The landscape around them is filled with chatter. Some of it can be heard; some of it must be sensed. Signals are being sent. Information is being exchanged. Like gossips tilting their heads in the direction of a juicy conversation, both men lean down, bending closer to a tobacco plant. ☒

Opposite: A wild tobacco plant grows on a burned site in southwestern Utah. It must deploy an arsenal of chemical weapons to keep voracious insects at bay. "It's remarkable that any part of the world is still green," says Baldwin.

(part 3)

Bad Genes, Good Drugs

Wondering what happened to all that knowledge we got from mapping the human genome? It launched a new race to identify the genes that give us diseases like high blood pressure, diabetes, and Alzheimer's. The winner gets to make remarkable new medicines

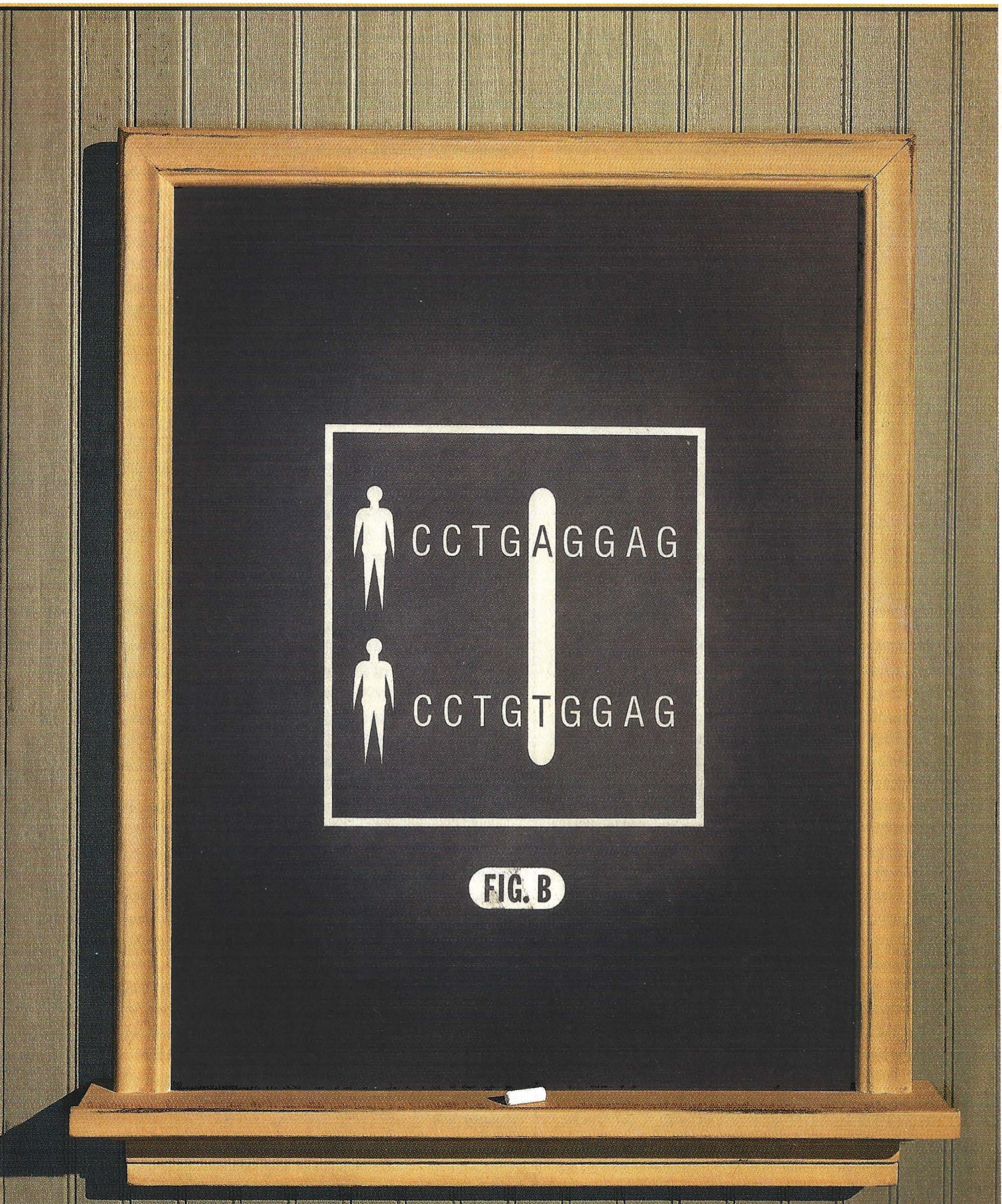
IN THE TINY WORKPLACE OF THE CELL, EVERY ONE OF OUR 30,000 genes has a partner. Each performs the same job, so to speak, as the gene in the office across the hall. Situated on paired chromosomes, these duos execute one small task, usually directing the assembly of a protein.

Now let's say that among the genes facing each other in the cell, there is a pair that runs a biotech company. Yes, biotech company genes. Let's call the firm that this gene pair directs Perlegen Sciences. Let's place this new company, shall we, in Mountain View, California, in the heart of Silicon Valley.

For Perlegen to function, the two genes that make up the pair must work well together. They should like and sympathize with each other, and like genes in a real cell, one should be able to stand in when the other is out. Let's name the two genes Brad Margus and David Cox. The former is the chief executive officer

Opposite: A single change in a gene, known as a single nucleotide polymorphism, can lead to disease. The top sequence shows a portion of the gene that codes for hemoglobin. The bottom sequence shows a base change—thymine (T) for adenine (A)—that alters the shape of the hemoglobin protein. Having two copies of the altered gene causes sickle-cell anemia.

BY JEFF WHEELWRIGHT • ILLUSTRATION BY DAN WINTERS & GARY TANHAUSER


CCTGAGGAG
CCTGTGGAG
FIG. B

and the latter the chief scientific officer of Perlegen Sciences.

Margus and Cox also happen to look and dress rather alike. Last fall at the company Halloween party, Brad went as David and David went as Brad, or so they joked afterward. But of course Margus and Cox aren't identical persons, just as paired genes in our cells almost never occur as perfect copies, because they were handed down by long and separate paths, one the mother's line and the other the father's. The genes have the same objective, which is spelled out in DNA's biochemical code of A's, C's, G's, and T's (for adenine, cytosine, guanine, and thymine). But rarely is the sequence of the letters, or nucleotides, exactly the same within each pair.

Letters can be shuffled, repeated, or deleted without losing their genetic meaning, the way that the word aeroplane is equivalent to airplane, for instance. The variations in spelling are known as polymorphisms. The most common and subtle type of polymorphism entails the substitution of a single letter. In English it would be kittykat instead of kittycat. In DNA dialect, if the nucleotide letter T appears instead of C, or G where usually there's A, the gene is said to contain a single nucleotide polymorphism. In short, a SNP (pronounced Snip).

Such variants have long histories. They first occur by chance on one chromosome of a person's genome, then either disappear when the person dies or get passed on to future generations. By convention, researchers use the term Snip for a variant that has been inherited by at least 1 percent of the world's population. If less frequent, the change is simply referred to as a mutation. Snips therefore tend to be old and common—survivors of evolution—while mutations tend to be rare, youthful additions to the genome, which may or may not take.

In a broad sense Snips are what cause human beings to differ—short people from tall people (because of Snips in the genes controlling height), black skin from white (because of Snips in the genes for pigment), and so forth. The single-letter changes underlie not only our physical diversity but also our different vulnerabilities to disease. Snips explain why under equal conditions some people will succumb to high blood pressure, asthma, or mental illness, and some people won't.

To return to the Perlegen pair, Margus and Cox, you could think of them as variants, or Snips, of each other. That fits, because the aim of their new company is to search for actual Snips in the human genome. Since the full human genome was first sequenced almost two years ago, the hunt for Snips has become the next new thing. Competing with other players in the biotech and pharmaceutical industries, Perlegen wants to discover significant Snips in the hope that new drugs will eventually flow from the knowledge.

Although the big promise of the Human Genome Project—drugs customized to a person's genetic profile—is still a long way off, the first step toward that goal is to understand the fine print of genetic diversity. The two groups that produced rival sequences of the genome—the National Human Genome Research Institute, run by the federal government, and Celera Genomics, a private company—have both set their sights on Snips.

Margus and Cox voiced confidence, as they glanced at each other in Perlegen's conference room, that their own effort would succeed. Their confidence stems from a powerful new technology called the microarray, or gene chip. The chips can scan whole genomes for changes in lettering, and Perlegen's chips have been hard at it for a year.

RECENTLY, COX AND MARGUS GAVE A PRESENTATION ON THE ROLE OF Snips in human disease. Margus, 41, set up his laptop on the conference table. He ran through the slides he normally uses for potential investors: the basic speech, not too technical. As Margus talked, Cox, 55, his hands clasped behind his head, interjected scientific detail. Jarrett, Margus's 13-year-old son, watched, too. He was in a wheelchair. Thin and shy, with neatly combed hair, the boy smiled but did not speak. He listened to the presentation with an almost furious concentration.

The first thing we learned about the human genome is how extraordinarily long it is: 3.2 billion nucleotide letters. A book containing the human genome sequence would have a million pages of text—3,200 letters per page.

Margus's next image showed strings of letters unspooling from the snapshots of five Perlegen employees (Cox among them). The DNA from each picture read "ATTGCAAGGCCGT," etc. But the five sequences, as Margus pointed out, were not quite the same. At one or two places in the sequences—called bases—there were differences in spelling. These bases marked Snip sites. Still, "All humans share 99.9 percent the same spelling," Margus said.

OK, this raised several questions. A frequent misperception is that the human genome announced by Celera and by the government team was *the* human genome. It wasn't. The two sequences were a kind of mishmash. Celera Genomics had blended the DNA of five people in order to derive one genome, and the government group had combined genetic samples from 24 people. The sequences represented the "canonical human being," as Cox put it. They were benchmarks—reference texts against which to compare the lettering of other genomes in other individuals.

Then what about the statement "All humans share 99.9 percent the same spelling"? It was imprecise, Cox admitted. Take any two people in the world, such as Brad Margus and his wife, and on average their genomes will be 99.9 percent identical. Snips, the major source of variation, occur roughly once every thousand bases—which is not very often. Still, the human genome is so long that there are millions of locations where the sequence of the letters is different.

But now take two other people, David Cox and Jarrett Margus. Although they are also 99.9 percent alike, the sites on their chromosomes where they differ are not the same sites as in the previous pair. Thus, each time another person's DNA is added to the equation, the overall similarity among the human genomes decreases. If we included the DNA of all 6 billion people on Earth, changes in lettering would show up at every base in the genome. "It's a conundrum," said Cox. "It's either we're 99.9 percent the same, or every base is different. You could say all humans share nothing, and that would be correct, too." →

Opposite: Brad Margus, gene chip in hand, stands with David Cox in the Perlegen lab in Mountain View, California. "I know better than anyone: You can't really celebrate just because you found the gene," says Margus.

'It's a conundrum,' said Cox. 'It's either we're 99.9 percent the same, or every base is different. You could say all humans share nothing, and that would be correct, too'

PHOTOGRAPH BY GILLIAN LAUB

'Each Snip tends to happen only once in the history of mankind. So

The question is more than semantic. At this early stage of discovery, the human genome is a murky and malleable document, open to interpretation. Like a new Web site, it's "under construction" by the scientists and companies seeking to develop it. Two genomes vary, or two genomes are alike, depending on the point of view, yet within a dozen genomes there seem to be common patterns to the variation. Blocks of Snips have been conserved over aeons of evolution, and these shared patterns may hold the clues to common diseases. Those are the variants Perlegen is after.

"Each Snip tends to happen only once in the history of mankind," Cox said dramatically. "So focusing on Snips is a way of using mankind as one big family."

But we were getting ahead of the lecture. Margus, waiting to continue, clicked on the next slide in the presentation. It was titled "Genetics and Disease." His son was swaying slightly in the wheelchair, his eyes cast down.

There was a list of the rare, infamous disorders that are caused when a single gene goes awry: cystic fibrosis, Huntington's disease, muscular dystrophy . . .

The most relevant condition wasn't cited, however: ataxia-telangiectasia, or A-T. It is a neurological disorder. In addition to a loss of motor control (ataxia), patients have cancer-prone immune systems. Spidery blood vessels (telangiectases) sprout in their eyes. A-T is caused by the failure of a gene by that name. Of the eight A-T genes present in the conference room that day—each person there bore two copies—at least three of the copies were flawed. A single change in the lettering was the culprit, but this was technically a mutation, not a Snip, because it is so terribly rare.

BRAD MARGUS IS NOT FROM THE WORLD OF SCIENCE. IN THE LATE 1980S, having earned a degree from Harvard Business School, he ran a shrimp-processing company called Kitchens of the Oceans, on the coast of Florida. In 1987 he and his wife, Vicki, started a family. They had a son, Colton, followed in short order by Jarrett and a third son, Quinn.

The two younger boys learned to walk and talk at a normal age, but they wobbled when they ran and slurred their words. They were diagnosed with ataxia-telangiectasia in 1993. It turned out that Brad happens to be a carrier of the A-T genetic disorder, and so is Vicki.

A-T is a recessive condition inherited according to the pattern established more than a century ago by the monk Gregor Mendel. Each parent carries both a bad copy and a good copy of the gene. The good copy keeps the parent healthy. It generates adequate amounts of a protein called ATM, which normally monitors and repairs damage to the cells' DNA. Without it, a series of small internal breakdowns will progress to serious disease. The Marguses' oldest child is healthy because he also received one good copy.

But by the unlucky odds of one in four, both Jarrett and Quinn inherited the two bad copies that their parents carried. There are no treatments for the condition.

After making contact with other A-T families, Brad and Vicki started a foundation, the A-T Children's Project, to raise money for research and to create notice for the disorder. They were interviewed on national television by Barbara Walters, and Brad testified before Congress. Margus was not satisfied with knowing the basics of his kids' disorder—he wanted every single molecular detail. He found scientists to tutor him in biology. With the foundation's money, he supported geneticists trying to uncover the location and identity of the A-T gene, which in the early 1990s remained a mystery.

Margus learned of a prominent geneticist who'd recently been hired by Stanford University. He flew to California, hoping to enlist the doctor as head of the foundation's scientific advisory board. But David Cox, although impressed by Margus's command of the subject, said he had his own research to manage. He codirected the Stanford Human Genome Center, which was gearing up for its part in the effort to sequence the entire genome.

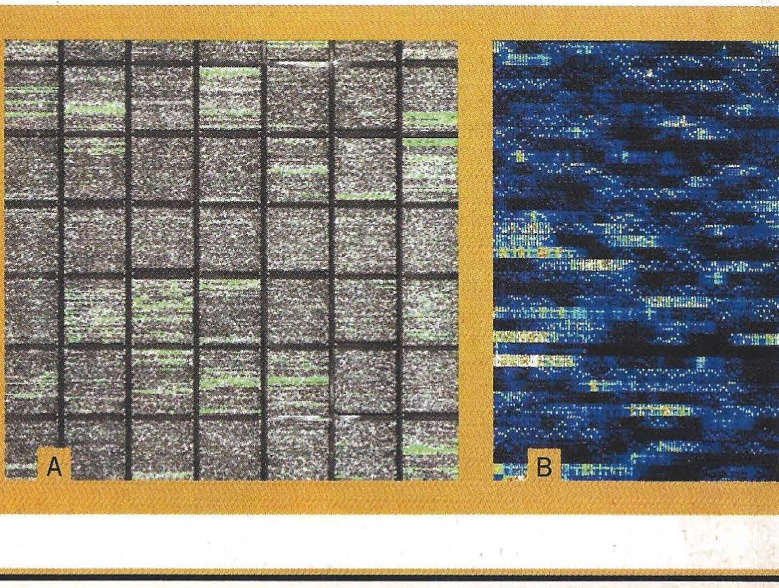
"He gave me a compassionate smile but said no," Margus recalled. "I talked to him for another hour, explaining why it wouldn't take too much of his time—all I needed him for, I explained, was his brains and advice. By the end of the meeting, David agreed to be my director."

Cox's career, like Margus's, was in transition. He had acquired

PHOTOGRAPHS COURTESY OF PERLEGEN SCIENCES (2).

HOW GENE CHIPS FIND SNIPS

Chemical letters, or bases, in a single strand of DNA will bind to their chemical partners: A to T, T to A, C to G, and G to C. This principle allows the Perlegen Sciences' gene chip to detect subtle variations in the human genome that may yield clues to the origins of complex diseases. (A) The chip, which is five inches square, is lined with about 60 million short, chemically synthesized single strands of DNA. These strands are called probes. (B) Each small square on the chip contains 400,000 probes. (C) This example shows how probes detect differences between two sample strands. When each letter in the DNA strand to be tested binds to its complement on the probe, the probe lights up, showing the strand's sequence. Because groups of single-letter variants (Snips, shown in red) are inherited together, finding one member can locate the group.



focusing on Snips is a way of using mankind as one big family'

a Ph.D. in genetics and then his M.D. His initial work, on the clinical side of medicine, was tending children with genetic disorders. "I was a pediatrician dealing with diseases I didn't understand," he said. "Next, I was involved in discovering single genes, for single-gene disorders. To which my wife [a genetics counselor] said, 'Ring me up when my patients should care.'"

She knew that although doctors might have a genetic test to offer, there wasn't much they could do after the diagnosis. The latest example was A-T, whose flawed gene was isolated in 1995, thanks partly to funds from the A-T Children's Project. Nevertheless, the physical condition of Jarrett and Quinn Margus continued to deteriorate, and by the late 1990s the boys were in wheelchairs. The research program that Cox had helped shape was no help yet.

In his studies Cox shed light on genes that contributed to Parkinson's disease and to a rare form of epilepsy, but increasingly he saw his work as "piecemeal contributions." "I realized," he said, "what I'm doing is not enough. Is genetics going to do anything useful or not?" Participating in the Human Genome Project began to give him a sense of the big picture and of the potential of genomics.

Meanwhile, Margus, still in Florida, studied precisely what goes wrong in the A-T gene sequence. He and Vicki had a fourth child, Caden, who was healthy, although he too was a carrier of ataxia-telangiectasia.

THE SLIDES FLICKERED ON THE LAPTOP SCREEN, MOVING FROM THE RARE disorders caused by rare mutations, like A-T, to humanity's more common diseases, which are believed to be connected to common polymorphisms—Snips.

"But the most common diseases," Margus read aloud, "are not caused by a single misspelling. . . . Most are probably caused by changed letters in 20 to 50 places contributing to 'complex' diseases such as Alzheimer's, diabetes, heart failure, schizophrenia, osteoporosis, asthma, lupus, multiple sclerosis."

These are the diseases of interest to the major drug companies and to Perlegen's rivals such as Celera. Explains Celera's chief scientific officer, Samuel Broder: "If you look at the top killers in the United States, they're not the classic Mendelian disorders. You have the interplay of 10 or more genes—a chorus of genes—in which any one gene is singing at a low volume. Plus, you have the environmental factors, which Mendel disallows or doesn't acknowledge are important."

By environment Broder means diet, lifestyle, cigarette smoking, chemical exposures, and other external factors, which influence risks for these complex ailments as much as family history does. Family history, for that matter, is an expression that doctors use when inheritance can't be calculated as simply as with the single-gene maladies. The more common but unknown genes of the Snip medical universe are called disease-associated genes, whose mechanisms will not be evident even when the genes are identified.

Finding these disease-associated genes will require radically new ways of sampling the genome. The conventional approach has been to look for one promising candidate, a gene whose protein might have an impact on blood pressure, say. First, you locate the gene, and then you study its function intensively.

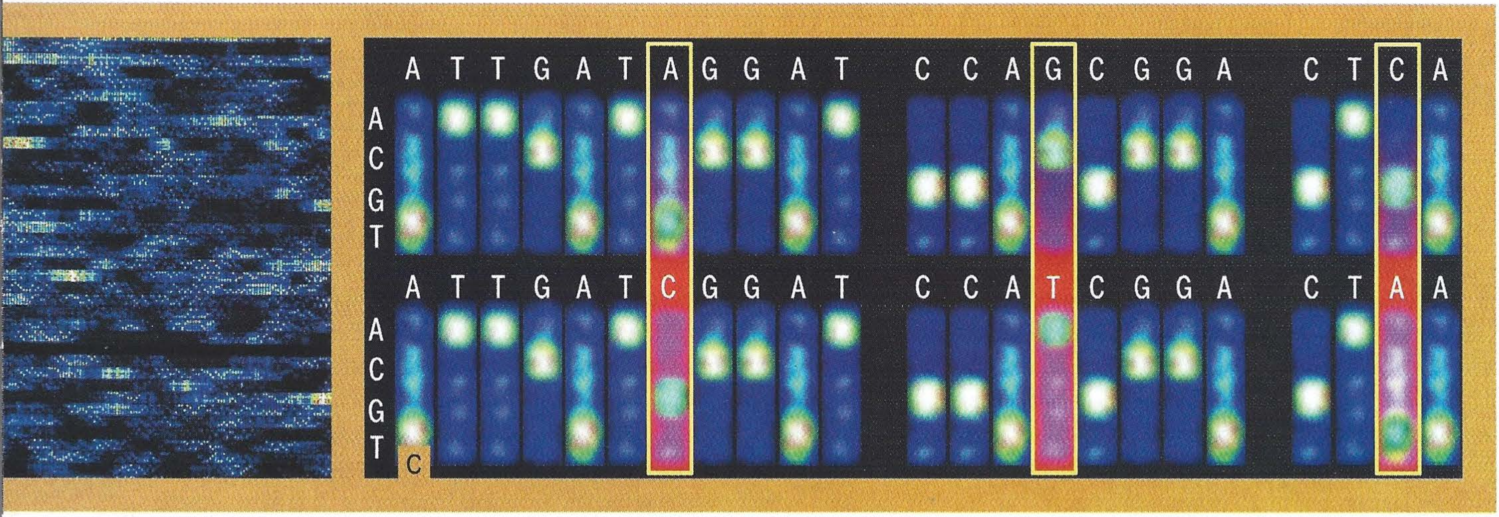
"This is the only way you could afford to do it until now," Margus said. "Most geneticists find a likely spot on the genome and get to work hunting."

The method has worked for pinpointing the sources of single-gene disorders like A-T, but it has not worked for elucidating complex, multi-gene disorders like high blood pressure. The contribution of any individual gene to the disease is too weak to be detected.

But researchers are betting they can simplify the search by focusing on blocks of Snips. Now the Perlegen presentation came to the point. "Snips occur together," said Margus. "We look only at places where genomes of people are frequently found to be spelled differently."

All right, so how will these chunks of Snips—called haplotypes—be identified? Margus introduced whole-genome scanning. The idea is that the haplotypes can be revealed by analyzing all the Snips simultaneously.

Scanning each letter of every subject's genome, however, is too costly and time consuming. So Perlegen planned a shortcut, taken from genomics—gene chips. The trick is to apply gene chips to a representative collection of human DNA. →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GRAPHIC BY MATT ZANG

> 'It was a conjunction of technological stars. The first was the Human Genome Project. The second was the chip technology, and the third was the software to join them together'

A MICROARRAY, OR GENE CHIP, CONSISTS OF MICROSCOPIC GRIDS OF DNA of known sequence. Normally, DNA is a double-stranded molecule, but on the chip it is laid down as a single strand. When exposed to a sample of unknown DNA, the probes on the chip bind to their complementary strands, thereby reading the sequences in the sample.

Genomics has brought "big science" into biology. Microarrays, DNA sequencers, and massively parallel computers have overturned the targeted approach to the genome by processing genes collectively. Machines can capture a cell's total genetic activity and then crunch the results for clues to disease. The amount of data is almost overwhelming. "It's a fire hose of information blasting people against the wall," said Cox.

In early 2000 Cox met with Stephen Fodor, the chief executive of a company called Affymetrix. Fodor had invented one of the two main types of microarrays. Affymetrix was now the dominant supplier of gene chips to the industry, but Fodor wanted to be more than a hardware salesman.

"Steve realized that this technology can scan the genome," Cox recalled. Microarrays would work faster and cheaper than the equipment Celera and the government group had used for their genome projects. Yet the Affymetrix chips were based on that output. The public sequence of the genome would serve as the DNA template for the microarrays. Then, by resequencing the genomes of other individuals, the chips could highlight the locations where the samples departed from the original. The bases of departure, of course, were the Snips.

Margus said, "What made David jump [from academia] was the technology."

"It was a conjunction of technological stars," Cox agreed. The first was the Human Genome Project. The second was the chip technology, and the third was the software to join the elements together."

The launch of Perlegen Sciences as a spin-off of Affymetrix was announced in October 2000. By the following spring $100 million had been raised for the venture. Cox was named chief scientific officer. When asked by Fodor to recommend a CEO, a person with solid business skills yet familiar with genetics, Cox soon thought of the right person. "He's a shrimp guy in Florida," Cox told Fodor, "but he is not your ordinary shrimp guy."

Today, Perlegen is about halfway through its scans of 50 genomes. The DNA samples were taken from previously established cell lines of 25 racially diverse individuals. On the face of it, that is too small a sample to reveal humanity's most meaningful variants. But Cox said, "The more common the change, the fewer people you need to test, statistically."

Within a few months the company expects to have found the haplotypes, or chunks of Snips, that occur most frequently. The expectation is that 300,000 blocks will emerge from the scans; each will be present in at least 10 percent of the sampled genomes. By the same token each is expected to occur in at least 10 percent of all human beings.

Firing a shot across the bow of the competition, the company's scientists published a report last fall on its scan of chromosome 21, the most detailed study of a human chromosome to date. Within 20 samples of the chromosome, the Perlegen group found some 35,000 Snips. But the variants could be organized in blocks: The four most frequent haplotypes were featured on 16 of the 20 chromosomes.

"That told us," said Cox, wrapping up the meeting, "that people are similar around the world in terms of these haplotype patterns."

Locating the Snips and haplotypes is actually the easiest part of the quest, a matter of applying the chip technology and reading what it spits out. Next, Perlegen and its customers will try to link the patterns to disease predispositions. Only if the genetic links stand up in large epidemiological studies will the third step be taken, which is to learn the biological functions of the disease-associated polymorphic genes. And the last step will be to devise new drugs against the new targets.

"It's like astrology," Cox said of the first step, "even if the genome is closer to biology than to the stars. But the value of the approach is that it poses hypotheses. Let's say there are 40 to 50 genes that have an effect on the risk of a disease, and you are able to find 20 of them. Now you have a better chance of doing something about it."

Margus wheeled Jarrett to the door of the conference room, where the boy softly said, "Bye."

"He's self-conscious about the slurring in his speech," Margus explained a few days later. "But that evening Jarrett asked a lot of questions. It was the first time he'd seen what Dad's company does. He asked, 'Can you tell who else has A-T by reading their genome?'"

Brad Margus has two tasks to reconcile: Snips and A-T research. "My passion is still A-T," he said. "I think about it falling asleep at night and in the shower the next morning. In this job I'm in the right place to *hear* things. To keep pushing on A-T from the inside, versus 'Here's this nice guy, head of a foundation,' on the outside looking in."

He has no illusions that Perlegen will solve his sons' problems. Still, his personal life has transmitted to his business life a sense of urgency. David Cox, for his own reasons, feels the same urgency.

"I have to know *something* sooner," Cox said. "The day that we'll know everything about genetic disease—you know what I say about that day? That I'll be dead."

"The attitude at Perlegen," Margus said, "is, 'If we made this experiment one day faster, could it help somebody's mother?' We only hire people who get it. It's not just about stock options. I've had my wake-up call in life, but others in the company have to have had theirs, too, in different ways." ☒

Opposite: Brad Margus sits between sons Jarrett (left) and Quinn at their home in Florida. Margus works at the Perlegen Sciences office in California and commutes back to his family two or three times a month.

PHOTOGRAPH BY GILLIAN LAUB

Marine Mammal
EMERALD

Do we kill whales with sound?

Darlene Ketten's fascination with how whales hear has swept her into a storm of controversy

BY SUSAN McCARTHY • PHOTOGRAPHY BY MAX AGUILERA-HELLWEG

Opposite: Darlene Ketten (in blue shirt) dissects out the left eye of this sperm whale for a colleague while others work on the brain and the nose.

THIS IS ONE OF DARLENE KETTEN'S MORE COMFORTABLE FIELD DISSECTIONS: THE SUN is out, there's a pleasant breeze, only one vulture looms overhead, and the whale doesn't stink. ¶ It's a small male sperm whale, only a year or two old—maybe 16 feet long if it were all here. Conveniently, only the head remains, at most a ton of blubber, skin, and bones resting on a wooden pallet. "You can lift it with a forklift! I love it," says Ketten, a biologist who studies the hearing of whales. Because this whale has been kept frozen, it is the freshest sperm whale she has cut into in years, and she can't help contrasting it with her last sperm whale dissection in 1999, on New Year's. She was at a party, "in velvet minidress and three-inch heels," when she got the call—a whale had beached and died on Nantucket Island. She dropped everything and got on an airplane. The whale stank horribly. She and her team dissected the ears and returned to the airport. On the way home everyone smelled so bad they were put on another plane by themselves, Ketten recalls.

Her subject this day had stranded on a beach in the Gulf of Mexico months earlier. Bathers poured water on him and covered him with their towels, but he was too sick to return to the sea, too big for any wildlife rehabilitation center. To end his misery, he had to be killed. Because his peripheral veins had collapsed, it proved impossible to inject a mortal dose of sedative. Finally, a veterinarian administered a local anesthetic, cut an artery, and let the whale quietly bleed out into the shallow water. Then the vet and a team from the National Park Service cut off his head, packed it in 150 bags of ice bought at a minimart, and trucked it to a walk-in freezer.

Now that head is surrounded by 15 scientists at the boat launch of the National Marine Fisheries Service Center in Fort Walton Beach, Florida. The researchers hope to solve a few of the mysteries of sperm whale anatomy. Wanda Jones, a Fisheries Service biologist, had the task of thawing the head—for three days. She's hoping that was enough.

Ketten begins by recording every possible dimension of the left side of the whale's head and jaw: position and size of the outer ear, size of the eye, distance between the center of the outer ear and the center of the eye, size of the blowhole, length of the jaw. As she finishes, the others join in the attack.

Ketten cuts through layers of blubber and muscle, searching for the tympano-periotic bulla, a bone complex that houses the middle and inner ear. She shows a dry specimen, smaller than her fist, taken from a whale that stranded in 1964. It may be hollow, but it is extraordinarily heavy. Ear bones of cetaceans—whales, dolphins, and porpoises—are the densest bones in the world, protecting delicate inner-ear tissues from damage and the tremendous pressure of dives. Sperm whales are thought to dive as much as a mile below the surface in search of squid and other prey.

The biologists wear a combination of medical and nautical gear, including surgical scrubs and rubber boots. They are piratical as they get into the flensing spirit. "Where are our butcher knives? Our big knives—where are they?" inquires Ketten, adding, "The art of flensing hasn't changed much over the past 100 years."

Blubber is surprisingly attractive: a spotless milk-white layer, inches thick, beneath the whale's deep, rich black skin. Beneath the blubber, Ketten finds jaw fats, creamy in color, far softer. When she tentatively identifies the shape of the casing that holds the fats, she says: "It's so cool! It's a sort of ovoid lobe of fat—if my theory is correct—that runs along the jaw, conducting sound waves." She describes the lobes as shaped like a pair of rabbit's ears, one on each side of the jaw.

As dusk falls, she reaches the ligaments behind the bulla and calls for a flashlight. Cutting it loose, she holds it up for all to admire before injecting it with formalin to preserve the cochlear structures inside. "It's a rock that has really delicate membranes in it," she says.

On the second day, the biologists tip the head over with a forklift so they can work on the other side. Ketten injects methylene blue dye into the outer ear, a slit about a third of an inch wide and shaped like a sound hole on a violin. The dye travels less than two inches before it hits an obstruction, possibly a lump of wax and dead tissue similar to those Ketten has seen in other whales. The canal may be a blind pouch, a useless relic of the whale's ancestry as a land animal. Ketten says she will examine it "slowly, tediously, carefully" in the laboratory to figure out whether it has any function.

Next, she saws out a block of tissue that contains the middle and inner ear so it can be put through a CT scanner, membranes intact. When the block finally comes loose, she peers into the space behind the ear and points out the enormous auditory nerve that passes through a hole in the skull from the brain to the ear. The nerve is big not only because whales are big; it is big because hearing is a whale's most important sense.

CETACEANS DESCENDED FROM LAND ANIMALS 50 MILLION TO 60 MILLION years ago. Gradually losing their legs, they evolved into ocean dwellers in a dim world where sound serves them better than light. As a result, their hearing developed far beyond ours, while their eyesight deteriorated—some river dolphin species have no functional lenses in their eyes and can register little except light and darkness. While humans have 38 optic nerves for every auditory nerve, the sperm-whale ratio is one-to-one. Instead of relying on eyesight, sperm whales use sound—to keep track of one another, announce the discovery of food, and cry in distress. Many cetaceans also use sound to echolocate. By uttering high-pitched sounds and listening to how

KETTEN HAS SHOWN THAT LOBES OF SOFT FAT IN A WHALE'S HEAD CAN PICK UP SOUND WAVES AS THE MAMMAL MOVES THROUGH THE WATER

the sounds bounce back to them, they can navigate lightless waters, find prey, and detect objects with phenomenal precision. The changes in the cetacean ear, head, and brain that have heightened this sense are a triumph of adaptation.

Nevertheless, whales also display vulnerabilities that humans are just beginning to understand: Sometimes they leave the water and strand themselves on a beach, where, more often than not, they die. Researchers know that strandings occur because an animal is ill, injured, or old. They are now worried that more and more of the injuries are caused by human behavior. The noise made by freighters in crowded shipping lanes, by underwater drilling and explosions, and by sonar devices used to hunt for submarines may be damaging whales' ears.

DARLENE KETTEN NEVER WANTED TO SPEND HER DAYS HOLDING PRESS conferences or giving interviews about marine mammal politics. With a joint appointment at Woods Hole Oceanographic Institution and Harvard Medical School, she studies the anatomy of cetaceans. Among researchers, already a cautious lot, she is legendary for her meticulous collection of data. She would be quick to point out that supporting hypotheses is inherently slow, cumulative, and incremental work. In her field there's a paucity of data about whales and dolphins to draw on because, she points out, "You have to wait for a volunteer." As a consequence, "It takes me millennia to get things out because I won't publish on a specimen number of one."

The data she has gathered so far from those limited sources have been maximized by a breakthrough she made in 1980, when she was studying for a doctorate at Johns Hopkins. Confronted by her first whale ear blocks, chunks of tissue similar to that cut from the sperm whale in Fort Walton Beach, she couldn't decide where to slice. So she visited the radiology department to ask if an X ray might locate the ear. They suggested a CT scan instead. The density of whale bones created problems, but eventually Ketten perfected a technology that worked, transforming the study of whale anatomy and even human cochlear implantation. (See "The Ketten Connection Between Whales and People," below.) The advantage of CT scans is that researchers can manipulate them endlessly to produce cross sections at different points and from different angles. Material of different densities can be removed from the image to show only bone, only muscle, or only fat.

In the scans, Ketten was able to see structures and fine details of the whale ear that had never been observed before. Because cetaceans have evolved so that their outer ears do little if any work, researchers had suggested that jaw fats receive sounds. Ketten was the one who put forth convincing evidence that the soft fat shaped like a rabbit's ear in a whale's head will pick up sound waves as the mammal moves through water and carry the waves to the middle and inner ear. "This particular type of fat has an acoustic impedance that's similar to seawater," she says, referring to cetaceans affectionately as "acoustic fatheads."

While the structure of cetaceans' middle and inner ears is similar to that of land mammals, including humans, Ketten has found differences that allow whales and dolphins to hear higher frequencies than they otherwise might, improving their ability to echolocate. She has determined that cetaceans can hear much higher and lower frequencies than humans because they have evolved a bigger range of widths and stiffnesses in the basilar membrane in the cochlea of their inner ears. →

THE KETTEN CONNECTION BETWEEN WHALES AND PEOPLE

In 1986, when Darlene Ketten was working at Harvard, she happened to overhear a conversation about cochlear implants in a hallway. "They were saying, 'Well, we can't get good scans because of the metal implant,' and I said, 'Yes, you can.'"

Much of a cochlear implant is made of platinum, a dense element that plays havoc with scans. As dense as platinum is, it's not much denser than cetacean ear bones, which had been a problem Ketten had to overcome in her scans. Soon she began consulting with implant teams at Harvard's Massachusetts Eye and Ear Infirmary and at the Washington University School of Medicine in St. Louis.

Cochlear implants restore partial hearing for some people who are profoundly deaf but whose auditory nerves are intact. The implant is an array of electrodes that functions in place of the cochlea. After the array is surgically placed in the inner ear, it is connected to an external device that does the listening the outer and middle ear ordinarily do, turning sound waves into electrical impulses and transmitting them to the electrodes, which then stimulate auditory neurons.

Inner-ear anatomy varies significantly from person to person, so surgeons must decide in each case where to place the implant, how to avoid damaging nearby features such as the facial nerve, and even which ear to operate on. Positioning the implant correctly is critical. With her ability to read scans involving dense material and visualize complex three-dimensional structures, Ketten was able to help surgeons decide before surgery where electrodes should be placed, and where, after surgery, they finally landed, so that audiologists could figure out which sound frequencies to assign to each electrode in the array.

This work continues to unfold: A recent study by Ketten and her colleague Margaret Skinner, a research audiologist at Washington University, showed that the farther into the cochlea the electrode array is implanted, the better the patient's ability to recognize spoken words.

Ketten's work on humans has also contributed to her cetacean research. "A lot of my work on marine mammals is in pathology, postmortem work," she says, "and that's something I learned in my work with human patients: to look at diseases or describe traumas using scans." —*S. M.*

Ketten also discovered that cetacean ears fall into three anatomic groups based on their lives in the water: "The frequencies they hear tell you something about what's important to them in their environment."

For example, odontocetes—toothed whales and dolphins—come in two flavors. Type I odontocetes hear upper-range ultrasonics, peaking above 100 kilohertz, about 80 kilohertz higher than human ears can hear. These animals include species such as the Amazon dolphin, which navigates in narrow spaces and clouded waters. Type II, the lower-range ultrasonic odontocetes, peak below 80 kilohertz. They are creatures of the coast and the open sea, needing lower frequencies to echolocate over longer distances in the search for, say, herring. There's something of a trade-off involved: Higher frequencies give precise images in echolocation; lower frequencies travel much farther but miss very small objects. Over the years Ketten has demonstrated that more than a dozen species that weren't previously known to echolocate have the capacity.

Ketten calls a third group Type M, for mysticetes, animals such as baleen whales that feed in the open sea on huge schools of krill and small fish. Their hearing and vocalizations are the least well known because they live far out at sea and tend to strand less often. The structure of their ears indicates they're adapted to using low frequencies, peaking between 10 hertz and 35 kilohertz, and apparently don't use echolocation. How they find their food without it isn't known. There is evidence suggesting that their lowest calls can be detected thousands of miles away, across the basin of an ocean.

So little is known about so many species of whales and dolphins that Ketten becomes frustrated when she is pressured by environmentalists and government agencies to give definite answers. She grumbles that "marine mammalogy is a field in which the plural of anecdote is data." And although she is eager to study the blocks of tissue she cut from the Fort Walton Beach sperm whale, she has had to put much of that work on hold to focus on the most demanding, high-profile case she has ever undertaken: 16 whales that beached in the Bahamas two years ago.

MOST WERE BEAKED WHALES, AND THEY STRANDED IN THE PROVIDENCE Channels in the northern Bahamas. At the time, the U.S. Navy was testing tactical mid-frequency sonar in the area. Six of the whales died. Ten were pushed back to sea and may have survived. The deaths—and the possibility that sonar was responsible for them—triggered a controversy that is still unsettled.

Sonar is simply man-made echolocation. Researchers often use the terms *dolphin sonar* or *bat sonar* as a shorthand for echolocation. Humans use sonar to navigate, fish, hunt for shipwrecks, and detect quiet modern submarines. There is little doubt that if sonar is intense enough, it can harm any living thing in its path. Some researchers speculate that some dolphins and whales use intense blasts of sound to blast fish or squid into insensibility. The Navy's sonar during the test reached 235 decibels at the source—underwater decibels are calibrated on a different scale from airborne decibels. At 180 decibels (underwater), human lung tissue begins to bruise.

Sent to investigate by the National Marine Fisheries Service, Ketten found hemorrhages in the ears and in the acoustic fats of five beaked whales she examined. Although pressured, Ketten refused to jump to conclusions at a press conference because she hadn't finished her analysis and hadn't yet seen the data on when and where the sonar had been active. "I'm still not ready to say the Navy did it," she told reporters.

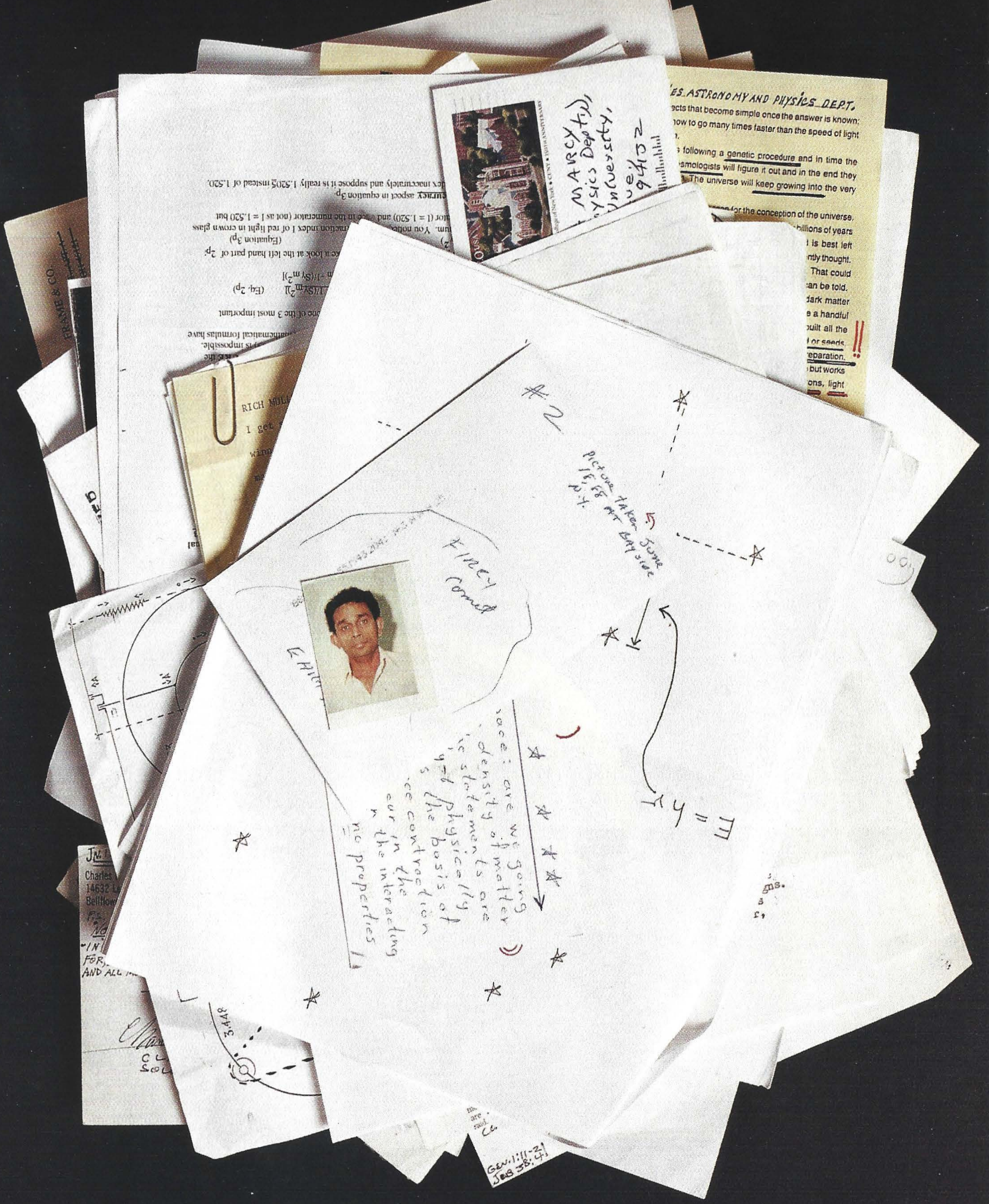
She emphasized that injuries to the ears of the whales did not kill them, although those injuries presumably caused them to strand. "They didn't die from the damage to their ears," she says. "They died from being on the beach for hours and hours." She did conclude that the injuries were consistent with acoustic or impulse trauma and contributed to an interim report put out jointly by the Navy, the Fisheries Service, and the National Oceanic and Atmospheric Administration last year. The report concluded that the tactical sonar was the "most plausible" source of the injuries to the whales' ears. The report recommended research to prevent incidents in the future, including identifying beaked-whale habitats and learning what sounds they make and use—precisely the sort of work Ketten wishes she had more time to do.

Determining whether any sea creature's death is caused by humans is an enormously difficult task. Ketten points out that she doesn't even have a database of what normal whale ears look like. Nobody is certain yet whether man-made noise is harming cetaceans, but researchers are trying to figure out which noises might be worse than others, how they do damage, and how the damage can be mitigated. Ketten says so much attention is being paid to the sonar threat that the far more widespread issue of ship noise has been neglected. Shipping lanes around the world are crisscrossed by enormous tankers broadcasting low-frequency noise that may be harming whales every day. She compares the problem of ship noise for whales to industrial noise for humans. Not only do many people work in harmful levels of industrial noise but countless people flock to rock concerts so loud they cause permanent and significant hearing loss. She wonders if dolphins seen bow riding near ships are doing something similarly foolish.

While some sounds may cause physical harm, there may be others that cause more subtle damage. "If you're an animal and you're breeding," says Ketten, "and somebody does the equivalent of scratching their nails on a blackboard, it may have an impact on your breeding." Noise pollution may also mask signals animals need to hear. If cetaceans can't communicate over long distances because a smog of sound intervenes, they might not be able to locate mates.

Ketten says solutions will not come easily: "Everyone wants a literal sound bite: 'This is safe.'" There may not be frequencies that are safe for all animals. "What's safe for a dolphin may not be safe for a seal," she says. "It's important to do this testing, and it's important to mitigate. I think sailors are a precious commodity just like marine mammals." If there is a balance to be struck between whales and people, one of the two will have to learn a lot more about the other first. ☒

Opposite: Despite an assault by researchers on this young sperm whale's frozen head, no one is certain why the animal stranded. He was neither thin nor injured, but he had been separated from his mother and his herd.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Letters from crank theorists—often handwritten or manually typed, exhaustively diagrammed, up to a hundred pages long—have inundated university science departments for years. Neel Shearer, the graduate assistant who filters physicist Stephen Hawking's e-mail, says that Hawking receives "hundreds of letters a month, at least, mostly theories about how the moon doesn't rotate, why gravity doesn't exist, how to go faster than the speed of light."

Notes from a parallel ~~world~~ ~~galaxy~~ universe ~~cosmos~~ ~~continuum~~ ~~dimension~~

INSIDE THE X-FILES AT THE UNIVERSITY OF CALIFORNIA AT BERKELEY, THE LINE BETWEEN THEORY AND FANTASY, SCIENCE AND SUPPOSITION, STARTS TO DISSOLVE. THE AUTHORS OF THESE DISSERTATIONS ARE OBSESSED—AND SCIENTISTS ARE NEARLY AS OBSESSED WITH THEM

ELEVEN YEARS AGO EUGENE SITTAMPALAM WAS sitting in a hotel room on the Libyan coast when he stumbled, as if by fate, on the unified field theory of physics. "I was on an engineering project at the time, with hardly any social life," he says. "I would retire to my room after dinner. I would switch on the radio, relax at my table, and start doodling." The problem that occupied him has stumped physicists from Albert Einstein to Stephen Hawking: How to join together the profound yet disparate insights of general relativity and quantum theory. But Sittampalam's doodling, apparently, drew connections that the rest had missed. "One thing led to another," he says, "and before the evening was over, I had the inverse square law of gravity derived—for the first time ever—from first principles!"

Sittampalam has no advanced degrees in physics. His theory is girded by mathematics no more complicated than high school algebra. Still, his claims are modest compared with those of other "maverick theorists," or cranks, as most scientists call them. At the American Astronomical Society meeting in 1999, a freelance astronomer argued strenuously that connecting certain pulsars across the night sky made an arrow that pointed directly to a vast alien communications network. A few years before, at Dartmouth, a dishwasher swamped the Internet newsgroups

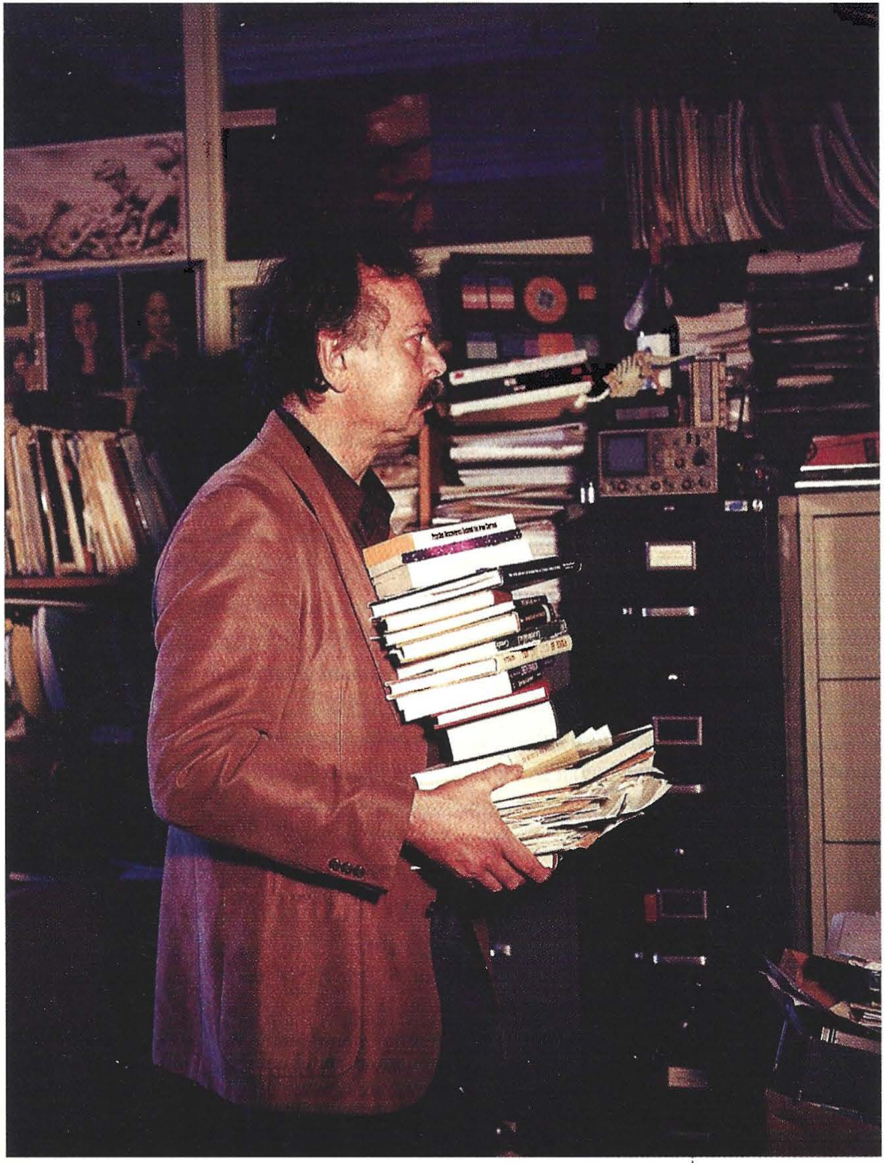
BY JENNIFER KAHN   PHOTOGRAPHY BY JIM GOLDBERG with his descriptions of the universe as a giant plutonium atom. The man, who identified himself as Archimedes Plutonium, wrote songs praising this atom universe and also provided stock tips. When he appeared on campus, it was in a parka covered with equations like a necromancer's robe.

Judging from the reams of odd theories sent daily to science journals, universities, and researchers, science cranks are more prolific than ever. This is true despite a discouraging silence on the part of the recipients. The author of one atmosphere-based theory of gravity estimates that he has mailed 5,000 copies of his work to physicists over the past 15 years but received just two replies. Presentation is part of the problem. "GENTLEMEN ARE YOU INTERESTED IN SEPARATING VALUABLE CHEMICAL COMPOUNDS FROM THE SUNSHINE RAY?" demands one impatient correspondent. Crank papers are so consistent in their tics that they're sometimes hung on physics department bulletin boards and given ratings—with points awarded for bold type, multiple exclamation marks, and comparison of self to Newton, Einstein, or God. But a few, like Sittampalam's, are more difficult to dismiss.

Sittampalam holds a bachelor of science degree from the University of Ceylon and has spent 20 years consulting for a number of prominent global engineering firms. His 85-page treatise is formatted with flawless professionalism, and he has no history of psychological disorders. Yet since his "breakthrough" in Libya, Sittampalam has all but sidetracked his career in pursuit of his theory. He has repeatedly sent his treatise to universities, paid to self-publish the work in paperback, and lost "a small fortune in salary" by his own estimation. Seven years ago he even offered a $25,000 reward to any physicist who could refute his theory and, as he puts it, "slap me out of this obsession." So far, no one has come up with a sufficient rebuttal.

Such single-minded absorption is part of the mythology of science. It's no wonder, then, that scientists are nearly as fascinated by cranks as cranks are by science. "It's unnerving," says Geoff Marcy, an astronomer at the University of California at Berkeley. "It shows how easy it is to slip from healthy, even necessary, conviction into certainty and delusion. Plus, you realize that you don't always know which camp you're in." There's the rub. Science owes a good part of its success to its capacity to contend with doubt—to engage it, respond to it, and transform itself in the encounter. Yet there's rarely a point at which a good idea becomes clearly, incontestably a bad idea. Neurologist Stanley Prusiner spent 15 years arguing that a misfolded protein called a prion caused the brain decay associated with scrapie and mad cow disease. Researchers snickered at him. Evidence slowly accumulated in his favor, and in 1997 he was awarded the Nobel Prize in medicine. "It's like a ball on top of a saddle," Marcy says. "You can't listen too closely to the establishment or you'll never be creative. But if you don't listen enough, you fall over the edge."

Physicist Rich Muller tries to save every crank missive he receives. Other scientists find the letters both frustrating and fascinating: "No one ever compares himself to a minor genius. They're all Copernicus or Schrödinger."



I FIRST CAME ACROSS SITTAMPALAM'S THEORY IN the Berkeley physics department. There, for the past 20-odd years, the secretaries have diligently compiled what they call the X-files: the mother lode of crankiana. Kept in a three-foot-wide cabinet, the files contain hundreds of submissions, including one man's musical CD about thermodynamics and another's explanation of relativity and quantum mechanics spelled out on six postcards. Elsewhere on campus, researchers maintain what amount to branch libraries of the X-files. "I have an entire shelf of crank mail," MacArthur-winning physicist Rich Muller told me. "My favorite is a book written by a crank that includes all the letters she received from scientists."

Muller's office at Lawrence Berkeley Laboratory sits several hundred feet above the

One man, who called himself Archimedes Plutonium, described the universe as a giant plutonium atom. He wrote songs in praise of it and also provided stock tips

city, in a stolid cement building edged by eucalyptus trees. The lab's newly heightened security was in force, and I was allowed through the gate only after a lab employee turned up to vouch for my good intentions. When I arrived, Muller had everything laid out, fat folders of letters and textbooks stacked across half of a colleague's desk. "There was a poster of the universe," he mumbled, peering up at the room's highest shelf. "It was beautiful. I put it someplace special. Now I don't know where it is."

Superficially, Muller is a bit cranky himself. His hair is thin but mussed, and his office is a cave of overstuffed folders and yellowing articles tacked to a corkboard. He is the author, among other things, of the controversial Nemesis theory, which argues that a second sun caused the extinction of the dinosaurs, and a novel that explains some biblical miracles as clever but scientifically consistent sleight of hand. Muller corresponds with cranks and has thought enough about them to sort them into a fairly elaborate taxonomy. "The range . . . is quite broad," he says. At the top of his hierarchy are the merely misguided: retired engineers who have strayed from load-and-strain calculations into surmises about relativity. The bottom of the stack is hairier: the Mullerian estate of the super-crank. Some super-cranks are harmlessly delusional, others dangerously paranoid, but none are very good at listening—a trait that drives Muller bats. "You take the time to explain the mistake in their argument, and they just ignore the explanation," he says bitterly. "They don't realize how much time scientists spend coming up with ideas and rejecting them."

Cranks, of course, see it differently. In their view they are Davids fighting a Goliath. Sometimes their foes may be theorists who have gone too far ("Deception, horn-swoggling . . . Who are you fooling?" demands an opponent of string theory). Other times they are scientists—overeducated, institutionalized, hidebound—who don't dare go far enough.

This confusion over fundamental purpose is understandable, given that modern physics manages to seem at once simple and profoundly puzzling. Astronomers have only recently determined that a mysterious "dark energy" is forcing the universe apart, overwhelming the equally mysterious "dark matter" that seemed to be holding it together. Even gravity, faithful shepherd of falling rocks and fly balls, has recently gone to pieces: At small distances, it may not be constant at all. "Some of the ideas are incredibly counterintuitive," says Nima Arkani-Hamed, a Harvard physicist who specializes in theoretical particle physics. "And they're just getting more bizarre."

Arkani-Hamed himself believes that space contains seven extra dimensions we can't see because they're rolled up like very small window shades. His mannerisms, too, might seem suspect in someone with less impressive credentials. He talks faster than I can take notes, a kind of super-revved speech that still seems to fall frustratingly short of the speed of thought. "Certain traits of personality and character are . . . close," he admits. "The obsessive tendencies, the compulsion, the restlessness. It's not the same, but there's a resemblance." Then he adds, dryly: "A lot of scientists have traits that would be bizarre if not channeled into science. I know that's part of why cranks interest me."

AFTER SEVERAL DAYS OF READING THE X-FILES, I FELT AS IF I WERE ATTENDING school in a parallel universe. "It is imperative that we begin burning water as fuel!" one author urged. Others were more puzzling. A note written on a ripped sheet of notebook paper said only, "I contend the holes on the right side of these pants are not explainable by contemporary science." A few submissions aped the style of scholarly papers, including credentials: An outline for "Symmetrical Energy Structures in a Mega-dimensional Cosmology," for instance, came from the director of the Alpha Omega Research Foundation in Palm Beach, Florida. But most favored a more urgent style. Arguments crescendoed to uppercase type. Words, boxed and colored, squeezed together on the page like castaways on a homemade raft.

At times the grandiloquence was so ingenuous it was hard to hold much of a grudge. "Readers, stretch your imagination to the very limits!" the inventor of Wavetron theory implored. "Together we will batter back the barbarous hordes!" The boldface words in another paper, taken together, read nearly like verse: "The eye is low / Negative ground / Electricity compressed, dead calm, displacing space / No one knows the cause / displacing . . . / repelling . . . / Well I do." But not every crank is so poetic nor so benign. Arkani-Hamed described one author whose e-mails had become increasingly virulent. Another physicist refused to be quoted by name in this article, replying tersely: "There is no guarantee that all cranks are harmless." Still another described his feelings about cranks as "Neutral. With a touch of fear."

One case in particular has echoed down the years with the force of a small-town murder. In 1952 a man named Bayard Peakes turned up at the office of the American Physical Society at Columbia University with a gun. Peakes was frustrated at the society's rejection of his pamphlet, "So You Love Physics." Unable to find any physicists at the society's office, he shot and killed a secretary instead. (Just months before, ironically, the society had changed its policy to open its annual meetings to public speakers and accept *all* scientific abstracts—including another by Peakes that aimed to prove that the electron doesn't exist.)

The Peakes case was unique in degree but not in kind. Scientists have been heckled, cursed, and harassed at work (one crank faxed love letters to a department chair and forged the

Engineer Eugene Sittampalam has offered $25,000 to any physicist who can refute his unified field theory. "I found myself getting really angry," one cosmologist said after reading the paper. "It must have hit some real insecurity."

signature of another scientist at the bottom). A few have even had cranks turn up at their homes.

It was hard not to have these cases in mind when I began contacting writers from the X-files, using the information that came with some of the papers. For the most part the authors were elusive. Phones had been disconnected, e-mail addresses bounced. The few who did answer were single-minded. One retired commercial diver answered all my questions with an uninterruptible monologue on gravity (it pushes rather than pulls, he said). An elderly man in southern California called back half a dozen times, each time hinting at his latest discovery.

"With psychosis, there's a kind of pressure to push it out," John MacGregor, an expert in the "outsider art" produced by mental patients, told me. "Sometimes the manic-depressives don't even use periods. They don't want to stop writing!" The trouble starts when such zeal is spiked with paranoia. "Schizophrenics have a tremendous desire to prove that they're sane," MacGregor said. "It could be that they've adopted science in order to prove just how rational and intelligent they are." He paused. "If a paranoid schizophrenic decides that certain rays are emanating from the physics department, it could be dangerous. These are the people who might come in and shoot it up."

COMPARED WITH THE PEOPLE MACGREGOR DESCRIBED—EVEN COMPARED with some of the physicists I interviewed—Sittampalam was charming. On the phone from his home in Sri Lanka, he proved candid but not overbearing, with crisp, British-inflected English pleasantly free of run-on tendencies. He answered questions about his family (he has five brothers and has never married) and chatted easily about his current job at ElectroFlow, a Missouri-based start-up that helps companies optimize their power consumption. He maintained that his physics theories were quite accessible; indeed, he hoped to see them introduced at the high school level.

I liked Sittampalam enough to inveigle a physicist friend to read Sittampalam's paper, with the promise that he remain anonymous. I was secretly hoping the paper would have some merit, or if not, that it would contain a clear error: one that, recognized, would set Sittampalam free from his compulsion. But when my friend got back to me, the news was bad. "As I read this, I kept thinking: 'How hard can it be to prove that this paper is incontrovertibly wrong?'" he said. "But it is hard. Not because his ideas are right. They're not. But because he's created a self-consistent system of arguments."

Self-consistency is not in itself a valuable trait—the theory that aliens created Earth and continue to control its evolution is a self-consistent system—but it can make things hard to refute. "I'd love to find just one equation in here and say, 'We have observations proving that's not correct,'" the physicist said. "But there's no mathematical progression. He starts with some very basic equations from classical mechanics. He mixes, stirs, spends some time hypothesizing in a very general way about physics, and out pops another familiar equation: $E=mc^2$. But really, he's just waved his hands. He could never have gotten to that next equation if he didn't already know what it was—and he knew what it was only because other people had figured it out for him using the traditional framework of physics."

Reading Sittampalam's paper feels a bit like being in a hedge maze: Just when you think you're heading toward some grand, central idea—an explanation of the cosmological redshift, for instance—the discussion loops away for another, more distant destination. There is the matter of Earth, for example. Sittampalam claims that his theory is the only way to explain why Earth hasn't lost enough energy over the years to spiral into the sun. But a physicist who saw the paper wrote in to note that that's exactly what *will* happen—just billions of years from now. Sittampalam acknowledged that mistake but attributed it to a typo. He had mistakenly left the words "under perturbation" out of his hypothesis, he said. Revised, his theory now explained why Earth, subject to the gravitational pull of the rest of the planets, has never wandered out of its orbit.

"First, he's talking about gravitational radiation, which is a real but minute effect; now he's talking about the solar system being sensitive to small changes," the physicist said. "It's true that if you moved the Earth a little bit today, its position and velocity in a month would become quite different. But that doesn't mean the shape of the current orbit is going to fall apart. We have simulations showing just the opposite, actually: that the solar system is stable over an incredibly long timescale. But that's what I mean. Every error you find, he's just going to change the subject. It's never ending."

THE TRUTH, DISPIRITING AS IT MAY SEEM, IS THAT CRANKS ARE PRETTY much never right. "We'd love it if one of these guys were right," Arkani-Hamed says. "A revolutionary idea that works—great!"

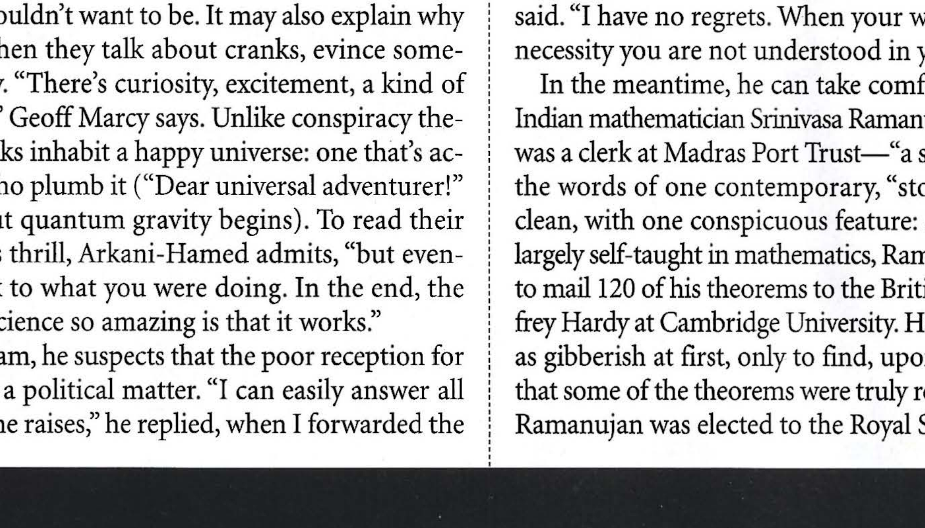
> 'If a paranoid schizophrenic decides that certain rays are emanating from the physics department, it could be dangerous. He might come in and shoot it up'

But real science tends to advance by increments rather than by revolutions. The life of working scientists is long on tedium and short on glory. They write grants, sit on committees, do paperwork. There is pressure to play it safe and be competitive. Cranks, by contrast, are free agents. With no career to lose and no scientific framework to restrict them, they can publish at their own pace and dare to shoot for the moon.

All of which may explain why most cranks aren't scientists and presumably wouldn't want to be. It may also explain why some scientists, when they talk about cranks, evince something close to envy. "There's curiosity, excitement, a kind of purity of purpose," Geoff Marcy says. Unlike conspiracy theorists, science cranks inhabit a happy universe: one that's accessible to those who plumb it ("Dear universal adventurer!" one postcard about quantum gravity begins). To read their ideas is a vicarious thrill, Arkani-Hamed admits, "but eventually you go back to what you were doing. In the end, the thing that makes science so amazing is that it works."

As for Sittampalam, he suspects that the poor reception for his work is largely a political matter. "I can easily answer all the critical points he raises," he replied, when I forwarded the physicist's critique. "But will he be convinced?" In the preface to his thesis, Sittampalam quotes Sir Martin Rees, a renowned astrophysicist and Astronomer Royal at Cambridge University. "Generally, researchers don't shoot directly for a grand goal," Rees writes. "Unless they are geniuses (or cranks) they focus on problems that seem timely or tractable." When I asked Sittampalam which he is, genius or crank, he was surprisingly equivocal. "Perhaps I'm a crank, but that's left for history," he said. "I have no regrets. When your work is for the future, by necessity you are not understood in your own days."

In the meantime, he can take comfort from the case of the Indian mathematician Srinivasa Ramanujan. In 1913 Ramanujan was a clerk at Madras Port Trust—"a short uncouth figure," in the words of one contemporary, "stout, unshaven, not over clean, with one conspicuous feature: shining eyes." Although largely self-taught in mathematics, Ramanujan had the audacity to mail 120 of his theorems to the British mathematician Godfrey Hardy at Cambridge University. Hardy dismissed the pages as gibberish at first, only to find, upon careful consideration, that some of the theorems were truly revelatory. Five years later Ramanujan was elected to the Royal Society of London. ☒


REPUBLIQUE TOGOLAISE
CENTENAIRE DE L'UNION INTERNATIONALE DES TELECOMMUNICATIONS
UIT
SOKODE

"Nothing new
under the sun
— Ec 1:3 —"
Xcuse paraphrase = Actually
it reads — NO NEW
THING UNDER THE SUN"
(QED)

"THE ORIGIN OF THE UNIVERSE
(AND MAN), CAME FROM LAWS
THAT WERE PUT IN MOTION
BY (THE) FIRST (AND UNCAUSED) CAUSE."

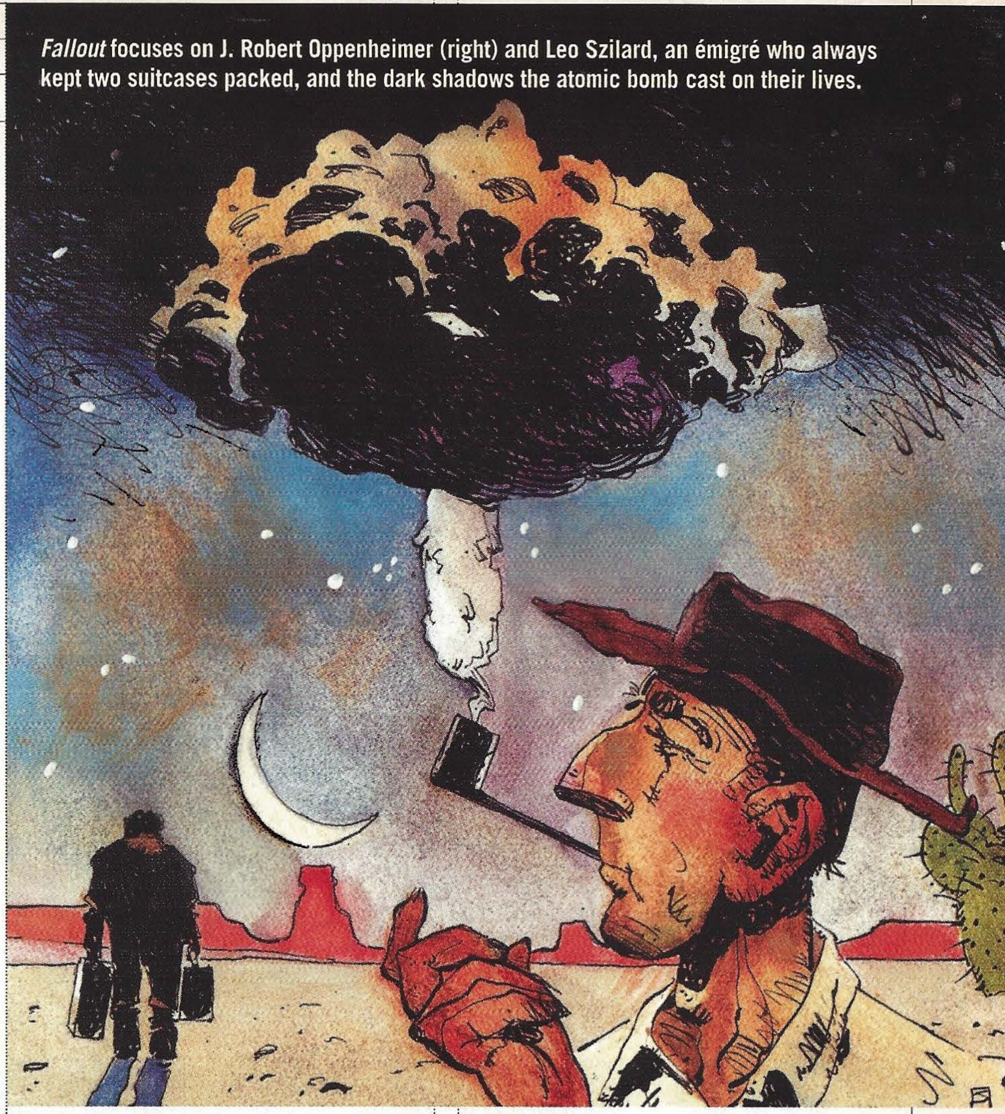
NO, VIRGINIA, THAT'S NOT "IVAN"
ON THE MOON! ITS NEIL!
GOD (STILL) FAVORS RIGHEOUS
WINNERS OVER OLIGARCHIES AND
DICTATOSHIPS! (QED)

Crank letters are so predictable in their grandiloquence that some physicists even rank them on a sliding scale. "There's something beautiful about the language," astrophysicist Saul Perlmutter says. Perlmutter tries to at least skim all the mail he receives. "It may be nonsensical, but often it's very evocative."

Physicists Who Built the Bomb, and Why They Hated It

Can a comic book change our perception of physics' greatest sin?

BY TIM FOLGER



Fallout focuses on J. Robert Oppenheimer (right) and Leo Szilard, an émigré who always kept two suitcases packed, and the dark shadows the atomic bomb cast on their lives.

IN THE SUMMER OF 1939, HUNGARIAN émigré physicist Leo Szilard visited another expatriate, Albert Einstein, at his summer home on Long Island. Szilard wanted Einstein to sign a letter to President Roosevelt urging that the United States begin work on developing an atomic bomb. Szilard, like Einstein a refugee from Nazi persecution, feared that Germany, with its many superb physicists, would build the bomb first. Einstein didn't need much convincing. A couple of months later, the fateful letter helped spur Roosevelt to commit the United States to the creation of a weapon of horrible and unprecedented power.

The task of directing the most daunting technical undertaking in history fell to physicist J. Robert Oppenheimer, the central figure in *Fallout*. Like *Maus*, artist Art Spiegelman's graphic chronicle of the Holocaust, *Fallout* is a comic book for sophisticated adult readers. Darkly evocative illustrations by Janine Johnston, Steve Lieber, Vince Locke, Bernie Mireault, and Jeff Parker are an integral part of author Jim Ottaviani's meticulously researched account of the Manhattan Project, America's desperate effort to build the first atomic bomb. In the right hands, comics can enliven history by conveying moods and details of character with cinematic immediacy. *Fallout*'s illustrators capture wordless exchanges among ambitious men, expressions of anger and despair. One series of panels shows the construction of the world's first atomic reactor, brick by brick, on squash courts at the University of Chicago. Where a written description might be tedious, the drawings are simple and unforgettable.

FALLOUT:
J. ROBERT OPPENHEIMER, LEO SZILARD, AND THE POLITICAL SCIENCE OF THE ATOMIC BOMB
By Jim Ottaviani, Janine Johnston, Steve Lieber, Vince Locke, Bernie Mireault, and Jeff Parker
G.T. Labs, $19.95

Fallout vividly depicts the immense toll exacted on all who labored on the Manhattan Project, of whom none suffered more than Oppenheimer. When the bomb was finally tested in New Mexico's isolated Jornada del Muerto (Journey of Death) Valley on July 16, 1945, Oppenheimer, who was over six feet tall, had turned into a wraithlike figure who weighed just 100 pounds. The book concludes with Oppenheimer's tragic postwar years, when the government revoked his security clearance, largely because of his support for arms control and past links to the Communist Party, links he had always freely admitted to. Although Oppenheimer went on to work at Princeton's Institute for Advanced Study, the public humiliation he endured after the war left him a visibly broken man.

One of the book's strengths is the detailed appendix of notes, in which Ottaviani takes pains to point out where he has created dialogue or incidents for the sake of his story. But with a cast of characters that includes Richard Feynman, Edward Teller, Enrico Fermi, and other towering figures of 20th-century physics, Ottaviani seldom needs to depart from the strict historical record. As Oppenheimer himself remarked, "Taken as a story of human achievement, and human blindness, the discoveries in the sciences are among the great epics."

After the war, Oppenheimer mused, "Physicists have known sin, and this is a knowledge which they cannot lose." One story line *Fallout* does not explore is Einstein's ambivalence about having encouraged the development of nuclear weapons. The end of the war found him vacationing in the Adirondack Mountains of New York. Upon hearing the news from his personal secretary of Hiroshima's destruction, he sighed in German, "Oh, *weh*"—alas.

ILLUSTRATION COURTESY OF JEFFREY JONES/G.T. LABS.

Fantastic Voyage

Exploring the Internet from the inside out

BY FENELLA SAUNDERS

IN THE DECADE SINCE TIM Berners-Lee, a software developer then at the CERN laboratory in Switzerland, created the first site on what he dubbed the "world wide web," the Internet has burgeoned into a ubiquitous presence in everyday life. Now more than half of all American homes have Internet connections that give them access to an estimated 2 billion Web pages. People take it for granted these days that they can reach remote corners of cyberspace in an instant, but few casual Web denizens know much about the technology that makes such fantastic armchair adventure possible. NetWorld, a 5,000-square-foot hands-on exhibit at the Museum of Science and Industry in Chicago, brings the inner workings of the Web to life.

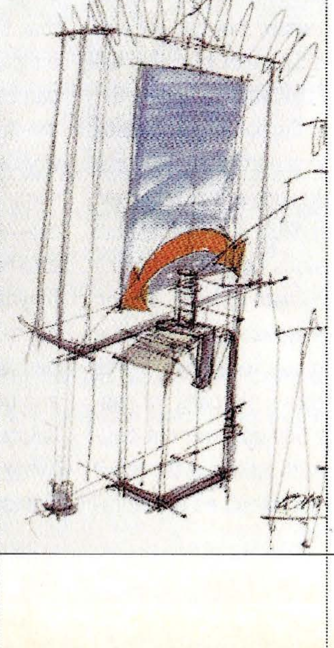
NETWORLD, AT THE THE MUSEUM OF SCIENCE AND INDUSTRY, CHICAGO (PERMANENT EXHIBIT)
www.msichicago.org/exhibit/networld/networld.html

Visitors are immediately immersed in a stream of 1s and 0s—projected on the walls, floor, and ceiling—and invited to dive into the digital bit stream that undergirds the Net. The first stop is a vending machine, where $2 buys a NetPass with an embedded microchip that activates your own personal digital self, a virtual sidekick that will shadow you throughout the exhibit. As a digital camera snaps your photo, this electronic stick figure pops up on a screen and immediately grabs your image and plasters it over its face.

Your digital self subsequently appears at each display in the exhibit when you wave the NetPass over a scanner. At the immense Portal Wall, 6 feet high by 30 feet long and made up of indigo-colored LCD screens, the NetPass triggers a spectacular view of the flow of digital data on the Internet. Your digital effigy appears on the left side of the screens and breaks apart into little pieces that become a stream of 1s and 0s—the bits that represent the most basic building blocks of data.

Another hands-on display shows how a message or data file is broken into segments—called packets—on its journey through the Internet. You select words on a touch screen to compose an e-mail message then watch as each word explodes into 1s and 0s before they are encapsulated within a pill-shaped packet. The color-coded, numbered packets then travel to another screen behind you, where other visitors can select them in the correct order to reassemble the message, much the way a computer does with an incoming e-mail.

One hands-on display (shown in a design sketch) uses a lever to trigger a graphic of data-transmission speeds.



The speed at which all this data moves depends largely on the bandwidth of the "pipe" it travels through. At one display, you can pull a large lever that graphically shows how quickly data moves through a typical 56,000-bit-per-second modem as compared with one of the Internet's main fiber-optic backbone cables—only a few dozen of these exist in the world—that carry 10 billion bits per second. To grasp the enormous difference in capacity, a wall panel invites you to imagine a drinking straw, then compare it to a tunnel two-thirds of a mile in diameter.

One display close to the end of the exhibit features a historical time line that chronicles the huge social impact the Internet has had during its relatively brief existence. The Internet had little direct influence on the lives of most Americans until 1994, when Netscape introduced the first Web browser. Yet today, more than 100 million people shop online each year, and Internet users send some 2 billion e-mails each day. Every time users log on, they entrust their most personal data to a system they can't even see.

That system includes "cookies," the small chunks of data that various Web sites place on users' computers to record their preferences or, more ominously, to track their movements on the Web. Your NetPass acts as a cookie. As you bid adieu to your digital self and prepare to leave the exhibit, a monitor indicates which displays you visited and when. But unlike the cookies on your computer, which can persist for years and keep all kinds of information on you, the museum doesn't save your data. In NetWorld, unlike most of the Internet, you can remain anonymous.

ILLUSTRATION COURTESY OF MUSEUM OF SCIENCE AND INDUSTRY, CHICAGO.

science best-sellers

1. **THE UNIVERSE IN A NUTSHELL**
   By Stephen Hawking, Bantam
2. **THE FUTURE OF LIFE**
   By E. O. Wilson, Knopf
3. **SYNAPTIC SELF: HOW OUR BRAINS BECOME WHO WE ARE**
   By Joseph Ledoux, Viking
4. **UNCLE TUNGSTEN**
   By Oliver Sacks, Knopf
5. **THE AUDUBON SIBLEY GUIDE TO BIRDS**
   By David Allen Sibley, Knopf
6. **THE BIRDS OF HEAVEN, TRAVELS WITH CRANES**
   By Peter Matthiessen, North Point Press
7. **SIX EASY PIECES, SIX NOT-SO-EASY PIECES**
   By Richard Feynman, Perseus
8. **THE MAP THAT CHANGED THE WORLD**
   By Simon Winchester, HarperCollins
9. **THE ESSENTIAL JOHN NASH**
   By John F. Nash, Edited by Sylvia Nasar and Harold Kuhn, Princeton University Press
10. **DON'T KNOW MUCH ABOUT THE UNIVERSE**
    By Kenneth C. Davis, HarperCollins

Source: Barnes & Noble Booksellers

books

The Eco-Warrior Writes Again

E. O. Wilson devises a new battle plan to save planet Earth

BY JOSIE GLAUSIUSZ

E. O. Wilson's new book pays homage to environmental activists, such as this tree-dwelling flautist who occupied a California redwood for 30 days to protest logging of old-growth trees.

PHOTOGRAPH BY PHIL SCHERMEISTER/CORBIS.

THE PETÉN REGION OF GUATEMALA, home to the brilliantly hued quetzal bird of sacred Mayan lore, was once a pristine expanse of tropical rain forest. Then in the early 1970s, Guatemala's military junta embarked on a road-building campaign, hoping to profit from logging and oil exploration. In the years since, half of the Petén's virgin forest has been slashed, burned, and destroyed. Meanwhile, some 6,000 indigenous families living in an area that has so far escaped deforestation have profited handsomely from the harvesting and sale of rain forest products, such as palm nuts and berries, allspice, potpourri, honey, handicrafts, and chicle, a natural form of latex. In *The Future of Life,* celebrated naturalist Edward O. Wilson reports that these people earn a combined annual income of $4 million to $6 million—more than could be gained by converting the forest into farms and cattle ranches. And if they can profit from protecting rather than plundering the forest, Wilson suggests, maybe others could reap similar benefits from environmental stewardship.

THE FUTURE OF LIFE
By Edward O. Wilson
Alfred A. Knopf
$22

The profit motive is not a traditional hallmark of the environmental movement. But Wilson, who won one Pulitzer in 1979 for *On Human Nature* and another in 1991 for *The Ants,* argues in his provocative new book that the future of life on Earth depends on figuring out profitable ways to reconcile the needs of the poor with the need to preserve biodiversity. Both situations are dire: Some 800 million people now live without sanitation and adequate food. Sadly, their search for land and freshwater can lead to deforestation and other forms of destruction, both of which are now driving species extinct so fast that if current trends continue, one-fifth of all animals and plants are expected to vanish by 2030. Half would disappear by the end of the century.

Wilson contends that this disaster can be averted by giving struggling nations and poor people the means to capitalize on conservation. For example, the EcoMaya program in the Petén brings ecotourists to schools in the region, where they can not only learn Spanish but also explore the Maya Biosphere Reserve. Carbon-credit trading is another profit-making enterprise, in which carbon-absorbing sinks such as newly planted forests are "sold" to polluting industries that need to meet emissions targets under the Kyoto Protocol on climate change. Wilson also advocates bio-prospecting—harvesting potential drugs from rain forest plants—as a source of local income. He calls for conservation groups to buy government contracts for land that would otherwise be leased to loggers and use it instead as a sanctuary. Breaking ranks with many other conservationists, he argues that the use of genetically modified crops, livestock, and farmed timber would increase productivity and thereby prevent further conversion of wildlands into cultivated farmland.

The viability of these proposals has yet to be proved. Critics argue, for instance, that the people most likely to profit from bio-prospecting are the pharmaceutical companies that comb the forests and fields of the developing world in search of the latest wonder drug. But it's hard to dispute Wilson's fundamental argument that the cheapest—and sanest—way to preserve species is to protect the natural ecosystems in which they now live. For this reason he pays tribute to the ground troops in the battle to sustain biodiversity: the protesters, picketers, and tree-dwellers whose loud shouts act as nature's early warning system. "They are the living world's immunological response," writes Wilson. "I say bless them all."

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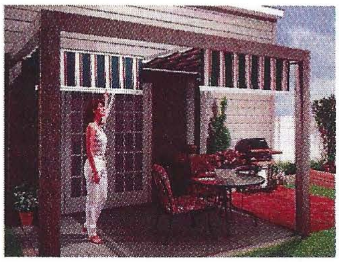

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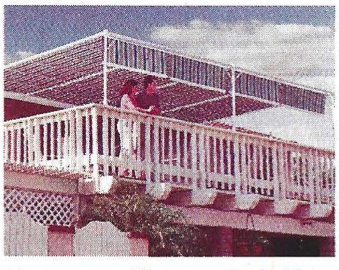

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toys

Brainy Bots

Build your own cardboard robot

BY FENELLA SAUNDERS

IF YOU THINK ROBOTS REQUIRE METAL bodies and silicon brains, think again. In The Ultimate Robot Kit, cardboard, paper clips, string, and glue are the primary materials you use to make the bodies and even many of the moving parts of some rudimentary robots. But don't let the low-tech approach fool you. These robots, which are powered by an AA battery and a simple motor that is included in the kit, feature some surprisingly ingenious mechanics that function like basic computer algorithms.

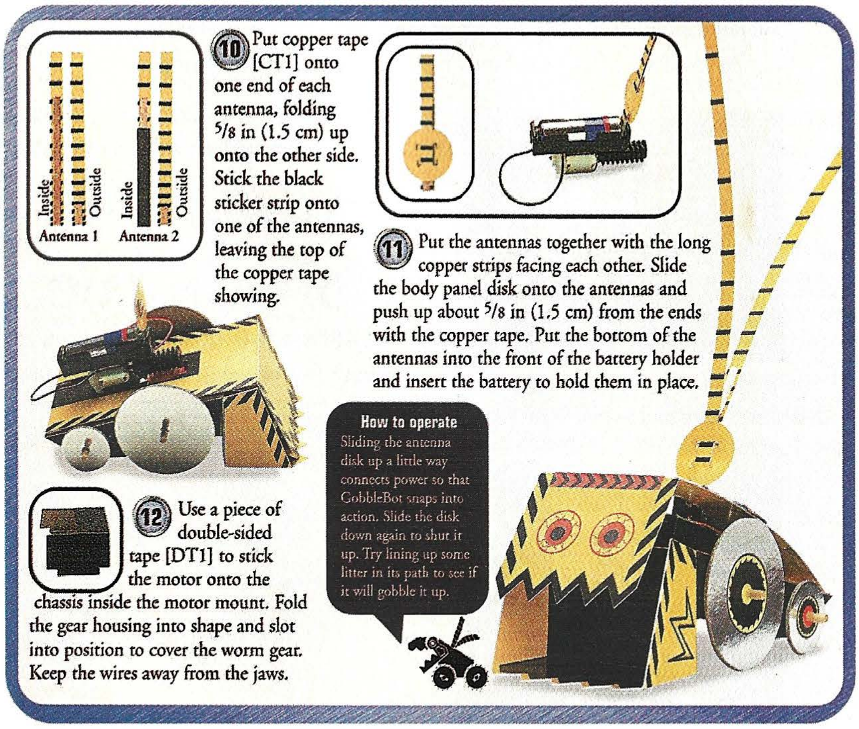
THE ULTIMATE ROBOT KIT
Dorling Kindersley
www.dk.com
$29.95

Of the four predesigned models included in the kit, the KnotBot is the best example of this sort of physical programming. When you tie a set of two-foot-long strings to this bright-yellow 3-by-6-inch robot, the knots in the length of the string behave like a simple program, telling the robot when to move left or right. The strings are tied to the spokes of the front wheels and threaded through notches on a cardboard "steering assembly." As the robot moves forward, the front wheel spokes wind up the draping string; when a knot hits a notch, the rear wheel jerks to one side and turns the robot. By changing the position of the knots, you can alter the sequence of turns and direct the cardboard robot to follow a completely different course.

Each of the three other predesigned robots in the kit has a signature mechanical feature. When a sensorlike disk on the top of BounceBot comes in contact with a wall or other obstruction, the robot body rotates and heads in another direction. The CreepycrawlyBot has an axle that moves its cardboard legs up and down in unison so it can lumber over obstacles in its path. The GobbleBot resembles a bulldozer; a turning cam opens and closes its maw so it can scoop up small objects. Finally, you can design and build your own DIYBot (as in Do It Yourself), with other included parts.

The real reward is that you're not just building models, you're actually programming robots—with no computer in sight.

The Ultimate Robot Kit comes with step-by-step instruction cards for each model, as well as a colorful booklet describing real-world robots that operate on the same basic principles.



⑩ Put copper tape [CT1] onto one end of each antenna, folding 5/8 in (1.5 cm) up onto the other side. Stick the black sticker strip onto one of the antennas, leaving the top of the copper tape showing.

⑪ Put the antennas together with the long copper strips facing each other. Slide the body panel disk onto the antennas and push up about 5/8 in (1.5 cm) from the ends with the copper tape. Put the bottom of the antennas into the front of the battery holder and insert the battery to hold them in place.

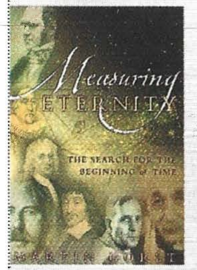
⑫ Use a piece of double-sided tape [DT1] to stick the motor onto the chassis inside the motor mount. Fold the gear housing into shape and slot into position to cover the worm gear. Keep the wires away from the jaws.

How to operate
Sliding the antenna disk up a little way connects power so that GobbleBot snaps into action. Slide the disk down again to shut it up. Try lining up some litter in its path to see if it will gobble it up.

we also like...

MEASURING ETERNITY: THE SEARCH FOR THE BEGINNING OF TIME

Martin Gorst
Broadway Books, $23.95



In 1649 James Ussher, an Irish Catholic bishop, declared that Earth was created by God at precisely 6 p.m. on October 22, 4004 B.C., a date accepted as gospel truth for many years. Gorst chronicles the efforts of Lord Kelvin, Sir Isaac Newton, Albert Einstein, Edwin Hubble, and other scientists to scientifically determine the age of Earth (4.5 billion years) and the universe (roughly 14 billion years).

CORPSE: NATURE, FORENSICS, AND THE STRUGGLE TO PINPOINT TIME OF DEATH

Jessica Snyder Sachs
Perseus, $25

The study of chronology is not limited to physicists and astronomers; it also preoccupies forensic scientists and other crime investigators. Sachs reveals how maggots on a festering body or dying leaves underneath a putrid leg bone can indicate the time of a murder. She also provides a historical survey of how biology, botany, and entomology have transformed forensics.

SECRET AGENTS: THE MENACE OF EMERGING INFECTIONS

Madeline Drexler
Joseph Henry Press, $24.95

Drexler argues that microorganisms, not humans, rule the world. In the wake of heightened concerns about anthrax and other potential weapons of bioterror, she contends humanity is in even greater danger from mutant strains of the normally mild influenza virus and even deadly bacteria lurking in the alfalfa sprouts at salad bars. Luckily, a host of epidemiologists and microbiologists are frantically working to avert disaster.

BRIGHT EARTH: ART AND THE INVENTION OF COLOR

Philip Ball
Farrar, Straus & Giroux, $27

The science of making pigments and dyes—accelerated by advances in chemistry—has given artists access to the fuchsias, crimsons, and ultramarines they required for their paintings, frescoes, textiles, and photographs. Ball documents the parallel development of the science and art of color through the centuries.

—Maia Weinstock

IMAGE COURTESY OF DORLING KINDERSLEY.

PEDIATRIC ASTHMA:

Research, awareness turn tide on disease

2002

by Carrie Hoppe
AAAAI Assistant Editor

Asthma affects more than 4.8 million children in the United States under the age of 18. Allergic diseases, which include asthma, are the most frequently reported chronic condition in children.

An immune system-mediated inflammatory disease, asthma is characterized by the narrowing and constricting of the muscles lining the body's airways. Common symptoms include coughing, wheezing, tightness of the chest and shortness of breath. Asthmatics' lungs are in a constant state of inflammation and susceptible to further inflammation, or "attacks," when exposed to environmental allergens, such as dust or mold, or irritants, such as cold, dry air. Asthma attacks, not treated properly or treated in time, can be fatal.

Presented by

AAAAI
AMERICAN ACADEMY OF ALLERGY
ASTHMA & IMMUNOLOGY

Who's at risk?

Anyone can develop asthma, at any time. However, recent reports suggest that asthma prevalence is about 50% higher among inner city children living in poverty than middle class children. Common characteristics of inner city environments – mold, cockroaches, dust mites and rodent droppings – are some of the most common allergens that trigger asthma symptoms.

In addition, children living in inner cities are more likely to be exposed to second-hand smoke, a potent asthma trigger. The National Cooperative Inner-City Asthma Study (NCICAS) showed that 59% of families had at least one smoker in the home, and 39% reported that the primary care provider is a smoker.

Psychosocial factors, such as social stress, can also have an impact on the development of and morbidity of asthma and allergic disease. "Studies have found that the stress of living in poverty, income issues and concerns about crime play a major role in increasing morbidity from asthma," said Peyton Eggleston, MD, FAAAAI, Professor of Pediatrics at Johns Hopkins Hospital in Baltimore, MD. The NCICAS study found that stress was associated with a 30% higher emergency department visitation rate.

Prevention may be possible

Some studies have found exclusive breast feeding for the first year of life, coupled with delayed introduction to potentially allergenic solid foods and cow's milk, might prevent "turning on" an allergic disease circuit in a child's body. Breast feeding may help protect a child's immune system from overreacting to these potential triggers until it is more fully developed.

Several studies have suggested that exposure to high concentrations of indoor allergens is associated with higher rates of asthma in children or an earlier age of disease onset. One study found the relative risk of asthma at age 11 to be 4.8 times greater if the child was exposed to high levels of dust mites in infancy. Other studies have found cockroach allergen, commonly found in inner city environments, to relate to the frequency of wheezing in children in their first year of life.

Early treatment makes a difference

New diagnostic and treatment techniques can help get a child's allergies and asthma quickly under control and potentially prevent a life-threatening allergic reaction or asthma attack. The allergist/immunologist, along with other healthcare professionals, is skilled in diagnosing allergic disease and asthma.

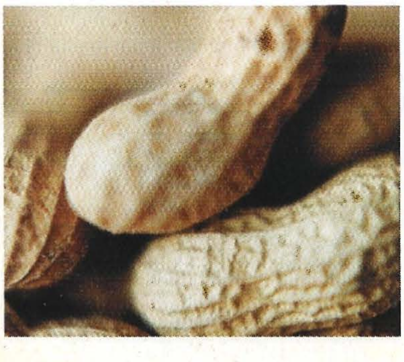
Most asthma treatment regimens include a daily dose of inhaled corticosteroids, supplemented by a rescue medication, or bronchodilator, to be used during attacks. The regular daily medication helps to keep airways open and reduce inflammation, avoiding potentially life-threatening asthma attacks when inflammation increases to the point of airway closure. Allergy medications also help to keep allergic asthma in check. Parental involvement and guidance is vital to keep a child actively taking medication and following prescribed control measures. One potential hurdle to a child's adherence to a treatment plan for asthma may be a parent's fear of side effects, such as growth retardation, from oral and inhaled corticosteroids, which are common asthma medications. The latest research indicates that inhaled corticosteroids may produce about a 1 centimeter decrease in growth in the first year they are used. This slight deficit seems to be made up in the child before growth is finished, resulting in an unaffected adult height, according to Gail G. Shapiro, MD, FAAAAI, AAAAI President and practicing clinician in Seattle, WA.

"This is very positive and comforting information. Oral steroids are usually used for short periods of time and do not cause permanent growth delay when used in this manner," she said. "Overall, the benefits of corticosteroids in controlling asthma and improving a child's quality of life far outweigh any negligible growth risks."

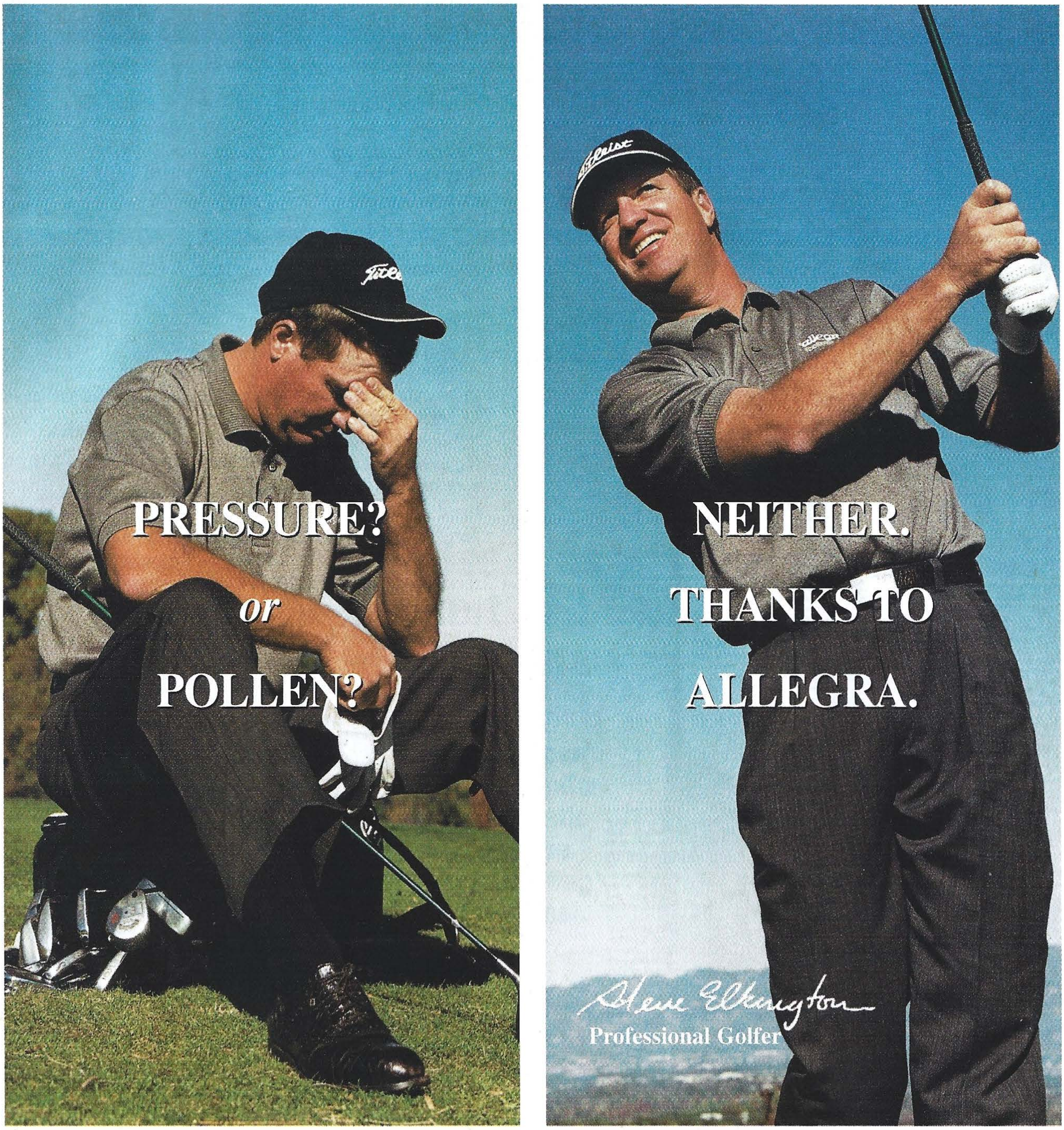
Research fosters new, better treatments

Many scientists believe that a number of genetic factors may interact with the environment to lead to the development of allergic disease and asthma. Researchers continue to search for the molecules in our environment that may interact with our genetic makeup in order to predict who may develop certain diseases and the severity of those conditions.

Another vein of research has concentrated on short-circuiting the allergic reaction in the body before it even begins. A new drug, that is already under review by the Food and Drug Administration (FDA), will mark the first-ever monoclonal antibody available for the ▸▸



Some studies have found exclusive breast feeding for the first year of life, coupled with delayed introduction to potentially allergenic solid foods and cow's milk, might prevent "turning on" an allergic disease circuit in a child's body.


PRESSURE?
or
POLLEN?
NEITHER.
THANKS TO
ALLEGRA.
Steve Elkington
Professional Golfer

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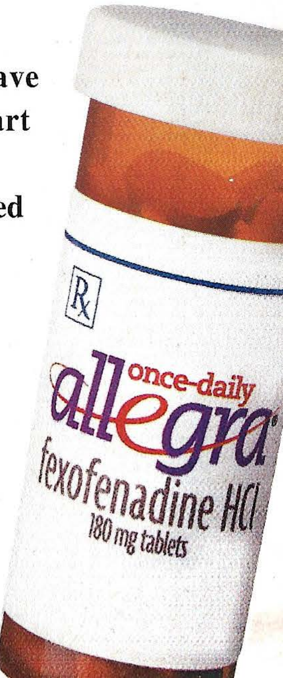
If you're one of millions who suffer from seasonal allergies, even a day of golf can leave you sniffling and teary-eyed. That's why once-daily Allegra can play an important part in treating your allergies. Only Allegra contains fexofenadine, an exclusive ingredient that provides long-lasting seasonal allergy relief without the drowsiness which can be caused by many antihistamines. So get back to your game. For people twelve and older. Side effects are low and may include headache, cold or back pain.

Talk to your doctor today about your allergies and free Allegra samples. For more information, call 1-800-allegra or visit allegra.com.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once-daily
allegra
fexofenadine HCl
180 mg tablets

Real relief. For real living.

PGA TOUR

Official Allergy Medication of the PGA TOUR **Please see additional important information on next page.**

Brief Summary of Prescribing Information as of November 2000

ALLEGRA®

(fexofenadine hydrochloride)

Capsules and Tablets

INDICATIONS AND USAGE

Seasonal Allergic Rhinitis

ALLEGRA is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 6 years of age and older. Symptoms treated effectively were sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes.

Chronic Idiopathic Urticaria

ALLEGRA is indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 years of age and older. It significantly reduces pruritus and the number of wheals.

CONTRAINDICATIONS

ALLEGRA is contraindicated in patients with known hypersensitivity to any of its ingredients.

PRECAUTIONS

Drug Interaction with Erythromycin and Ketoconazole

Fexofenadine hydrochloride has been shown to exhibit minimal (ca. 5%) metabolism. However, co-administration of fexofenadine hydrochloride with ketoconazole and erythromycin led to increased plasma levels of fexofenadine hydrochloride. Fexofenadine hydrochloride had no effect on the pharmacokinetics of erythromycin and ketoconazole. In two separate studies, fexofenadine hydrochloride 120 mg twice daily (two times the recommended twice daily dose) was co-administered with erythromycin 500 mg every 8 hours or ketoconazole 400 mg once daily under steady-state conditions to normal, healthy volunteers (n=24, each study). No differences in adverse events or QT_c interval were observed when patients were administered fexofenadine hydrochloride alone or in combination with erythromycin or ketoconazole. The findings of these studies are summarized in the following table:

Effects on steady-state fexofenadine hydrochloride pharmacokinetics after 7 days of co-administration with fexofenadine hydrochloride 120 mg every 12 hours (two times the recommended twice daily dose) in normal volunteers (n=24)

Concomitant Drug	C_{maxSS} *(Peak plasma concentration)*	$AUC_{ss(0-12h)}$ *(Extent of systemic exposure)*
Erythromycin (500 mg every 8 hrs)	+82%	+109%
Ketoconazole (400 mg once daily)	+135%	+164%

The changes in plasma levels were within the range of plasma levels achieved in adequate and well-controlled clinical trials.

The mechanism of these interactions has been evaluated in *in vitro*, *in situ*, and *in vivo* animal models. These studies indicate that ketoconazole or erythromycin co-administration enhances fexofenadine gastrointestinal absorption. *In vivo* animal studies also suggest that in addition to increasing absorption, ketoconazole decreases fexofenadine hydrochloride gastrointestinal secretion, while erythromycin may also decrease biliary excretion.

Drug Interactions with Antacids

Administration of 120 mg of fexofenadine hydrochloride (2 x 60 mg capsule) within 15 minutes of an aluminum and magnesium containing antacid (Maalox®) decreased fexofenadine AUC by 41% and C_{max} by 43%. ALLEGRA should not be taken closely in time with aluminum and magnesium containing antacids.

Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential and reproductive toxicity of fexofenadine hydrochloride were assessed using terfenadine studies with adequate fexofenadine hydrochloride exposure (based on plasma area-under-the-concentration vs. time [AUC] values). No evidence of carcinogenicity was observed in an 18-month study in mice and in a 24-month study in rats at oral doses up to 150 mg/kg of terfenadine (which led to fexofenadine exposures that were respectively approximately 3 and 5 times the exposure from the maximum recommended daily oral dose of fexofenadine hydrochloride in adults and children).

In *in vitro* (Bacterial Reverse Mutation, CHO/HGPRT Forward Mutation, and Rat Lymphocyte Chromosomal Aberration assays) and *in vivo* (Mouse Bone Marrow Micronucleus assay) tests, fexofenadine hydrochloride revealed no evidence of mutagenicity.

In rat fertility studies, dose-related reductions in implants and increases in postimplantation losses were observed at an oral dose of 150 mg/kg of terfenadine (which led to fexofenadine hydrochloride exposures that were approximately 3 times the exposure of the maximum recommended daily oral dose of fexofenadine hydrochloride in adults).

Pregnancy

Teratogenic Effects: Category C. There was no evidence of teratogenicity in rats or rabbits at oral doses of terfenadine up to 300 mg/kg (which led to fexofenadine exposures that were approximately 4 and 31 times, respectively, the exposure from the maximum recommended daily oral dose of fexofenadine in adults).

There are no adequate and well controlled studies in pregnant women. Fexofenadine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects. Dose-related decreases in pup weight gain and survival were observed in rats exposed to an oral dose of 150 mg/kg of terfenadine (approximately 3 times the maximum recommended daily oral dose of fexofenadine hydrochloride in adults based on comparison of fexofenadine hydrochloride AUCs).

Nursing Mothers

There are no adequate and well-controlled studies in women during lactation. Because many drugs are excreted in human milk, caution should be exercised when fexofenadine hydrochloride is administered to a nursing woman.

Pediatric Use

The recommended dose in patients 6 to 11 years of age is based on cross-study comparison of the pharmacokinetics of ALLEGRA in adults and pediatric patients and on the safety profile of fexofenadine hydrochloride in both adult and pediatric patients at doses equal to or higher than the recommended doses.

The safety of ALLEGRA tablets at a dose of 30 mg twice daily has been demonstrated in 438 pediatric patients 6 to 11 years of age in two placebo-controlled 2-week seasonal allergic rhinitis trials. The safety of ALLEGRA for the treatment of chronic idiopathic urticaria in patients 6 to 11 years of age is based on cross-study comparison of the pharmacokinetics of ALLEGRA in adult and pediatric patients and on the safety profile of fexofenadine in both adult and pediatric patients at doses equal to or higher than the recommended dose.

The effectiveness of ALLEGRA for the treatment of seasonal allergic rhinitis in patients 6 to 11 years of age was demonstrated in one trial (n=411) in which ALLEGRA tablets 30 mg twice daily significantly reduced total symptom scores compared to placebo, along with extrapolation of demonstrated efficacy in patients ages 12 years and above, and the pharmacokinetic comparisons in adults and children. The effectiveness of ALLEGRA for the treatment of chronic idiopathic urticaria in patients 6 to 11 years of age is based on an extrapolation of the demonstrated efficacy of ALLEGRA in adults with this condition and the likelihood that the disease course, pathophysiology and the drug's effect are substantially similar in children to that of adult patients.

The safety and effectiveness of ALLEGRA in pediatric patients under 6 years of age have not been established.

Geriatric Use

Clinical studies of ALLEGRA tablets and capsules did not include sufficient numbers of subjects aged 65 years and over to determine whether this population responds differently from younger patients. Other reported clinical experience has not identified differences in responses between the geriatric and younger patients. This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and may be useful to monitor renal function. (See CLINICAL PHARMACOLOGY).

ADVERSE REACTIONS

Seasonal Allergic Rhinitis

Adults. In placebo-controlled seasonal allergic rhinitis clinical trials in patients 12 years of age and older, which included 2461 patients receiving fexofenadine hydrochloride capsules at doses of 20 mg to 240 mg twice daily, adverse events were similar in fexofenadine hydrochloride and placebo-treated patients. All adverse events that were reported by greater than 1% of patients who received the recommended daily dose of fexofenadine hydrochloride (60 mg capsules twice daily), and that were more common with fexofenadine hydrochloride than placebo, are listed in Table 1.

In a placebo-controlled clinical study in the United States, which included 570 patients aged 12 years and older receiving fexofenadine hydrochloride tablets at doses of 120 or 180 mg once daily, adverse events were similar in fexofenadine hydrochloride and placebo-treated patients. Table 1 also lists adverse experiences that were reported by greater than 2% of patients treated with fexofenadine hydrochloride tablets at doses of 180 mg once daily and that were more common with fexofenadine hydrochloride than placebo. The incidence of adverse events, including drowsiness, was not dose-related and was similar across subgroups defined by age, gender, and race.

Table 1

Adverse experiences in patients ages 12 years and older reported in placebo-controlled seasonal allergic rhinitis clinical trials in the United States

Twice daily dosing with fexofenadine capsules at rates of greater than 1%

Adverse experience	*Fexofenadine 60 mg Twice Daily (n=679)*	*Placebo Twice Daily (n=671)*
Viral Infection (cold, flu)	2.5%	1.5%
Nausea	1.6%	1.5%
Dysmenorrhea	1.5%	0.3%
Drowsiness	1.3%	0.9%
Dyspepsia	1.3%	0.6%
Fatigue	1.3%	0.9%

Once daily dosing with fexofenadine hydrochloride tablets at rates of greater than 2%

Adverse experience	*Fexofenadine 180 mg once daily (n=283)*	*Placebo (n=293)*
Headache	10.6%	7.5%
Upper Respiratory Tract Infection	3.2%	3.1%
Back Pain	2.8%	1.4%

The frequency and magnitude of laboratory abnormalities were similar in fexofenadine hydrochloride and placebo-treated patients.

Pediatric. Table 2 lists adverse experiences in patients aged 6 to 11 years of age which were reported by greater than 2% of patients treated with fexofenadine hydrochloride tablets at a dose of 30 mg twice daily in placebo-controlled seasonal allergic rhinitis studies in the United States and Canada that were more common with fexofenadine hydrochloride than placebo.

Table 2

Adverse experiences reported in placebo-controlled seasonal allergic rhinitis studies in pediatric patients ages 6 to 11 in the United States and Canada at rates of greater than 2%

Adverse experience	*Fexofenadine 30 mg twice daily (n=209)*	*Placebo (n=229)*
Headache	7.2%	6.6%
Accidental Injury	2.9%	1.3%
Coughing	3.8%	1.3%
Fever	2.4%	0.9%
Pain	2.4%	0.4%
Otitis Media	2.4%	0.0%
Upper Respiratory Tract Infection	4.3%	1.7%

Chronic Idiopathic Urticaria

Adverse events reported by patients 12 years of age and older in placebo-controlled chronic idiopathic urticaria studies were similar to those reported in placebo-controlled seasonal allergic rhinitis studies. In placebo-controlled chronic idiopathic urticaria clinical trials, which included 726 patients 12 years of age and older receiving fexofenadine hydrochloride tablets at doses of 20 to 240 mg twice daily, adverse events were similar in fexofenadine hydrochloride and placebo-treated patients. Table 3 lists adverse experiences in patients aged 12 years and older which were reported by greater than 2% of patients treated with fexofenadine hydrochloride 60 mg tablets twice daily in controlled clinical studies in the United States and Canada and that were more common with fexofenadine hydrochloride than placebo. The safety of fexofenadine hydrochloride in the treatment of chronic idiopathic urticaria in pediatric patients 6 to 11 years of age is based on the safety profile of fexofenadine hydrochloride in adults and adolescent patients at doses equal to or higher than the recommended dose (see Pediatric Use).

Table 3

Adverse experiences reported in patients 12 years and older in placebo-controlled chronic idiopathic urticaria studies in the United States and Canada at rates of greater than 2%

Adverse experience	*Fexofenadine 60 mg twice daily (n=186)*	*Placebo (n=178)*
Back Pain	2.2%	1.1%
Sinusitis	2.2%	1.1%
Dizziness	2.2%	0.6%
Drowsiness	2.2%	0.0%

Events that have been reported during controlled clinical trials involving seasonal allergic rhinitis and chronic idiopathic urticaria patients with incidences less than 1% and similar to placebo and have been rarely reported during postmarketing surveillance include: insomnia, nervousness, and sleep disorders or paroniria. In rare cases, rash, urticaria, pruritus and hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnea, flushing and systemic anaphylaxis have been reported.

OVERDOSAGE

Reports of fexofenadine hydrochloride overdose have been infrequent and contain limited information. However, dizziness, drowsiness, and dry mouth have been reported. Single doses of fexofenadine hydrochloride up to 800 mg (six normal volunteers at this dose level), and doses up to 690 mg twice daily for 1 month (three normal volunteers at this dose level) or 240 mg once daily for 1 year (234 normal volunteers at this dose level) were administered without the development of clinically significant adverse events as compared to placebo.

In the event of overdose, consider standard measures to remove any unabsorbed drug. Symptomatic and supportive treatment is recommended.

Hemodialysis did not effectively remove fexofenadine hydrochloride from blood (1.7% removed) following terfenadine administration.

No deaths occurred at oral doses of fexofenadine hydrochloride up to 5000 mg/kg in mice (110 times the maximum recommended daily oral dose in adults and 200 times the maximum recommended daily oral dose in children based on mg/m^2) and up to 5000 mg/kg in rats (230 times the maximum recommended daily oral dose in adults and 400 times the maximum recommended daily oral dose in children based on mg/m^2). Additionally, no clinical signs of toxicity or gross pathological findings were observed. In dogs, no evidence of toxicity was observed at oral doses up to 2000 mg/kg (300 times the maximum recommended daily oral dose in adults and 530 times the maximum recommended daily oral dose in children based on mg/m^2).

Prescribing Information as of November 2000

Aventis Pharmaceuticals Inc.
Kansas City, MO 64137 USA
US Patents 4,254,129; 5,375,693; 5,578,610
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allb1100Aa

ALG-JA-232-1

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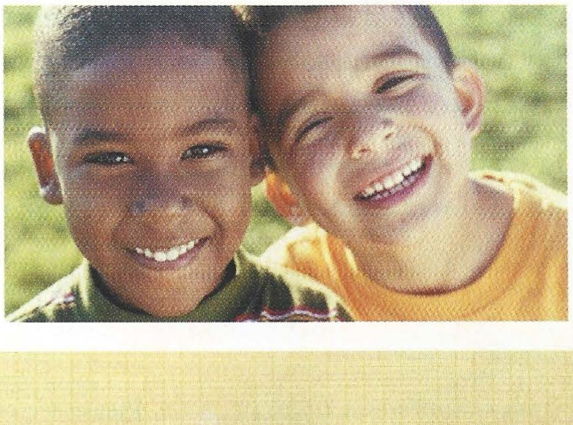
treatment of allergic disease. The new treatment regimen, known as anti-IgE, revolves around the theory that an imbalance in the immune system may contribute to the development of allergic disease. Anti-IgE therapy stops the allergic reaction before it starts, allowing the patient to avoid allergy symptoms, which also often trigger an asthma attack or lead to the development of asthma.

Researchers are exploring other targets for new allergic disease treatments. New drugs may zero in on cytokines in the body, which are thought to be responsible for maintaining the chronic inflammation seen in asthma, to inhibit or to block antibodies that trigger the allergic cascade. Additional therapeutic research may also lead to the development of new corticosteroids and new nonsteroidal anti-inflammatory drugs, which would retain the anti-inflammatory efficacy but offer fewer systemic side effects.

New approaches for monitoring asthma and allergies in children and delivery devices are also on the horizon. A new nebulized corticosteroid was released on the U.S. drug market recently that can be used in children as young as 12 months. Previously, such inhaled corticosteroid therapy was only available for children four years of age and older and typically administered via an asthma inhaler.

As the medical community takes greater notice of the growing threat of allergic disease, new research will lead to earlier medical interventions for children suffering from allergies and asthma, according to Donald Y.M. Leung, MD, PhD, FAAAAI, Professor and Head, Division of Pediatric Allergy/Immunology at National Jewish Medical and Research Center. "Research will likely lead to more effective and safer therapies for children with asthma and other immune-mediated diseases. It will also provide more awareness of the importance of earlier intervention in these illnesses," Leung said. "It is becoming quite clear that it is important to intervene early in order to prevent consequences that could become even worse later in life." ●

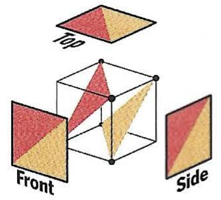


BY SCOTT KIM

MATHEMATICA REDUX

In the late 1950s IBM asked designers Charles and Ray Eames to create an exhibit for the Los Angeles Museum of Science and Industry. The result was *Mathematica*, a celebration of mathematics that endures to this day as a standout among science exhibits. Now permanently housed at the Boston Museum of Science, *Mathematica* was intended, in the words of Charles Eames, to enlighten the amateur without embarrassing the specialist. A traveling version of the exhibit is at San Francisco's Exploratorium through May 5. It will then move on to the California Science Center in Los Angeles, where it will be in residence from July 12 through September 3.

LOVE TRIANGLES



A sign in *Mathematica* reads: "Projective geometry is the study of geometric properties that are preserved by projective transformations." To illustrate, the Eames studio suspended an array of triangles so that they formed different designs when viewed from different angles. Shown at right are two colored triangles suspended inside a cubic frame and the views you would see from the front, side, and top.

Below are four pairs of views. In each case, eight colored triangles are suspended inside a cubic frame. Each triangle is the same color on both sides. Can you draw the third view for each cube? As in the pairs of views shown, all eight triangles are fully visible in the third view. Can you figure out how the triangles are arranged in the cube? Hint: Problems 1 and 2 are closely related, as are problems 3 and 4.

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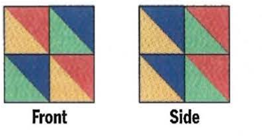

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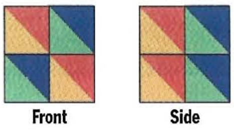

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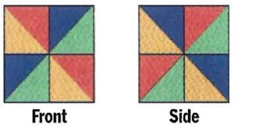

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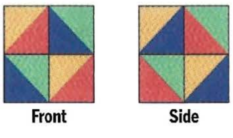
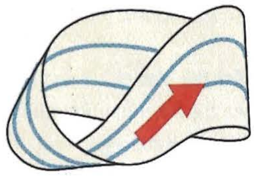
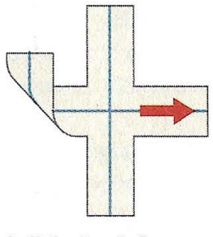


MÖBIUS STRIP

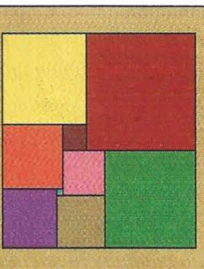
Mathematica features a famous loop with a twist, similar to the one above, which is named after the 19th-century German mathematician and astronomer August Ferdinand Möbius. A red arrow travels along a track that runs down the middle of the giant Möbius strip in the exhibit. Press a button, and the arrow crawls along the track, soon appearing on the underside of the strip. The arrow then continues in the same direction, returning ultimately to its starting point.

1. What would happen if you cut the strip in half along the track line?
2. Imagine that instead of one track down the middle, two tracks run side by side, dividing the strip in thirds, as shown in the figure at right. How many trains would be required to travel all the tracks?
3. What would happen if you cut the strip in thirds along the tracks?
4. Study the unfolded track below. Can you glue the ends together so that a single train could traverse all the tracks on both sides? Note: The train must go straight—it can't make a turn at the intersections. How could you glue the ends together so that two trains are required to traverse all the tracks? How about three trains? Can you connect the ends so that four trains are required to travel all the tracks?





SQUARE DANCE



This curious diagram hangs on a wall in the *Mathematica* exhibit. Nine squares, all different sizes, fit together to form a rectangle. This is the smallest number of squares that can appear in such a construction. Can you deduce the sizes of the squares in this diagram and in each of the diagrams at right? The squares have been stretched into rectangles to avoid giving away their relative sizes. All dimensions are whole numbers. Hint: Select two adjacent squares and call their edge lengths x and y. Express the sizes of the other squares in terms of x and y. Eventually, you will reach a point where the size of a square can be expressed two different ways, and you can resurrect your long-dormant algebra to solve for x and y. Choose the smallest numbers that work. Some squares in problem 1 are the same size. In the remaining problems, all the squares are different sizes.

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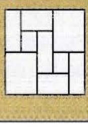

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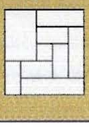

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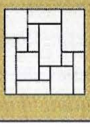

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The following books, journals, and Web sites provide additional information about topics featured in *Discover* this month.

10 R&D

"Silicon Goes Pow!" Mikulec, Frederic V., et al. "Explosive Nanocrystalline Porous Silicon and Its Use in Atomic Emission Spectroscopy." *Advanced Materials* 14 (January 2002): 38–41.

"Rogue Genes South of the Border." Quist, David, and Ignacio Chapela. "Transgenic DNA Introgressed into Traditional Maize Landraces in Oaxaca, Mexico." *Nature* 414 (November 29, 2001): 541–543.

"Night Owls vs. Early Birds." Learn more about sleep at the National Sleep Foundation Web site: www.sleepfoundation.org.

"By the Numbers." For more about Daniel Caton's research, see dancaton.physics.appstate.edu/Birthrates/AASstuff.

"Early Breath of Fresh Air." Phillips, G. N., et al. "Is the Redox State of the Archean Atmosphere Constrained?" *Society of Economic Geologists Newsletter* 47 (October 2001).

"Fetuses Take Air Pollution to Heart." For more, see Beate Ritz's page: www.ph.ucla.edu/class/epi/epi260/Ritz_home_page/Home_ritz.html.

"Ask the Wizard." To learn more about tinnitus, see the American Tinnitus Association's Web site: www.ata.org.

"Let There Be Light." Learn about the universe's early infrared glow at www.theastronomycafe.net. Also see Abel, Tom, et al. "The Formation of the First Star in the Universe." *Science* 294 (January 4, 2002): 93–98.

"20,000 Leagues Under." Vecchione, Michael, et al. "Worldwide Observations of Remarkable Deep-Sea Squids." *Science* 295 (December 21, 2001): 2505–2506.

"The Four-Minute Race Eraser." Kurzban, Robert. "Can Race Be Erased? Coalitional Computation and Social Categorization." *Proceedings of the National Academy of Sciences* 98 (December 18, 2001): 15387–15392.

"Atomic Merry-Go-Round." Sauer, J. A., et al. "Storage Ring for Neutral Atoms." *Physical Review Letters* 87 (December 31, 2001): 270401. See prl.aps.org. The Web site for Michael Chapman's group: www.physics.gatech.edu/ultracool.

Under attack by a hungry caterpillar, this tobacco plant can send out a chemical SOS, attracting parasitic wasps that prey on the multi-legged marauder. See page 46.

"Landmarks." For the text of the Biological Weapons Convention, see www.fas.org/nuke/control/bwc/text/index.html. For further information on U.S. opposition to the globally agreed inspection scheme, see: www.acronym.org.uk/bwc/revcon8.htm.

See the zoetrope whirring on the Web: easyweb.easynet.co.uk/~s-herbert/zoet.htm.

"Tributes." To learn more about Maureen Raymo's research, see scrippsnews.ucsd.edu/releases2002/cody_award_raymo.html.

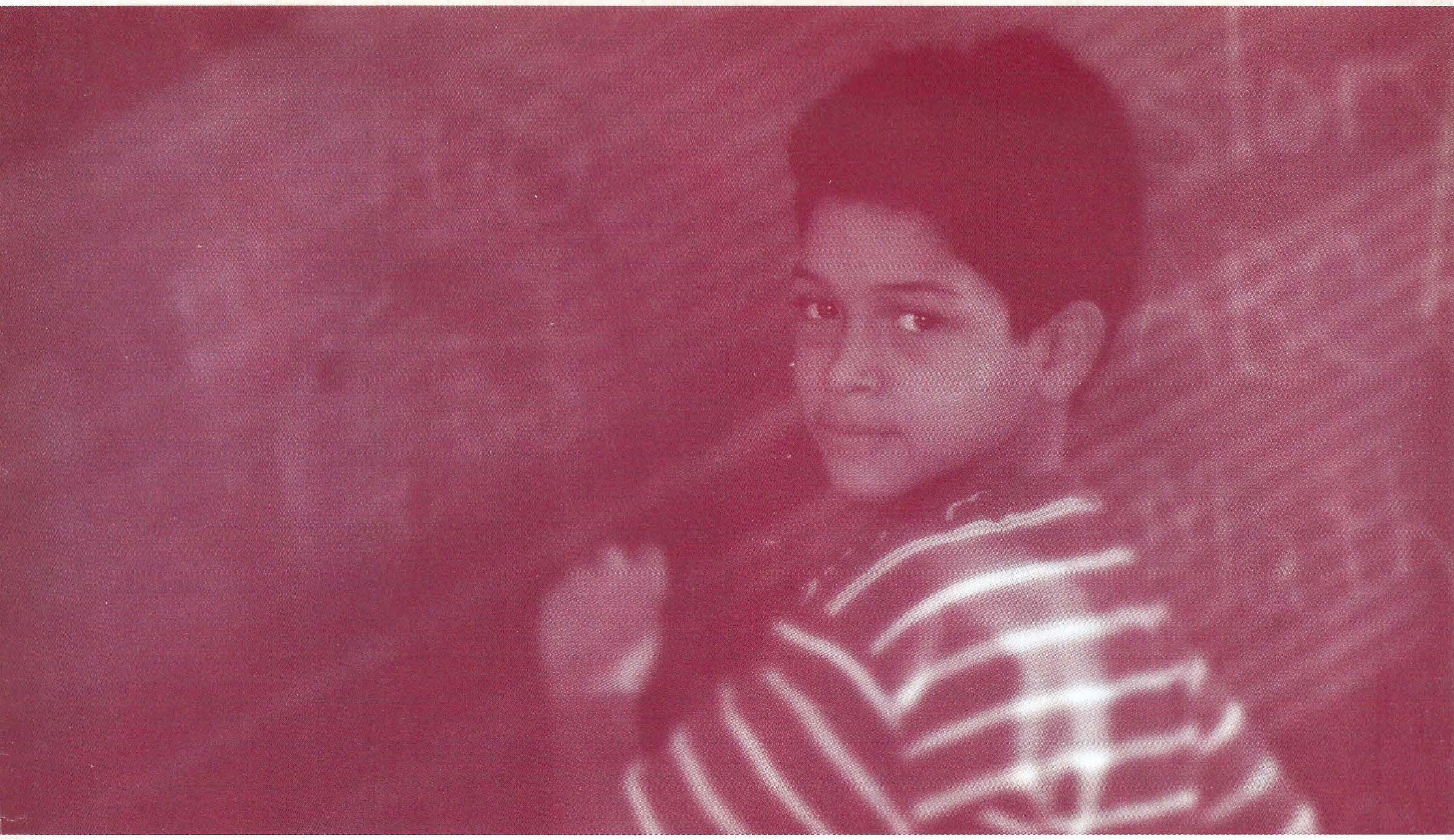
"Computers Enter the Molecular Zone." Bachtold, Adrian, et al. "Logic Circuits With Carbon Nanotube Transistors." *Science* 294 (November 9, 2001): 1317–1320. See www.sciencemag.org.

Huang, Yu, et al. "Logic Gates and Computation From Assembled Nanowire Building Blocks." *Science* 294 (November 9, 2001): 1313–1317. See www.sciencemag.org.

Lieber, Charles M. "The Incredible Shrinking Circuit." *Scientific American,* September 2001. See www.sciam.com.

Charles Lieber's Web page: cmliris.harvard.edu.
Cees Dekker's Web page: www.mb.tn.tudelft.nl/user/dekker/index.html.

PHOTOGRAPH BY MAX AGUILERA-HELLWEG



Asthma is nothing to play around with. But it doesn't have to sideline your child.

More than 5 million children have asthma, making it the most common chronic childhood illness. Untreated, or improperly treated, asthma can limit social or athletic activities, cause school absences and even result in death.

If your child shows the following symptoms, he or she may have asthma:

- Coughing, either constant or intermittent.
- Wheezing (an audible whistling sound) when your child exhales.
- Shortness of breath, rapid breathing or chest tightness.
- Getting tired easily, stopping play or becoming easily irritated.
- Problems sleeping because of coughing or difficulty breathing.
- Infants may have problems feeding and may grunt during suckling.

An allergist/immunologist can evaluate your child and determine the best treatment options. Visit the Physician Referral Directory at www.aaaai.org to find an allergist/immunologist near you.

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Cees Dekker's carbon nanotube transistors won a 1999 Discover Award for Emerging Technology. See "The Smallest Switch," *Discover,* July 1999, p. 104. Available at www.discover.com/99awards/emerging.html.

"Old Disease in the New World." Read about Jerry Conlogue and mummies at www.ebmedia.com/mummy/aboutronandjerry.html.

"*Discover* Dialogue." Jeffrey Sachs's Web site is www.cid.harvard.edu/ciddirector. Also see Dixon, Simon, et al. "The Impact of HIV and AIDS on Africa's Economic Development." *British Medical Journal* 324 (January 26, 2002): 232–234. Available at www.bmj.com. A summary of the WHO Commission on Macroeconomics and Health report can be found at www3.who.int/whosis/cmh/cmh_press/e/who_hq_20Dec2001.htm.

"Follow-Up: Who'll Watch the Neutrinos?" See the Super-K home page: www.phys.washington.edu/~superk.

19 FUTURE TECH

David Smith and his colleagues at the University of California at San Diego explain their work on left-handed materials: www-physics.ucsd.edu/lhmedia.

Two recent papers in *Science* give more information: Wiltshire, M.C.K., et al. "Microstructured Magnetic Materials for RF Flux Guides in Magnetic Resonance Imaging." *Science* 291 (February 2, 2001): 849–851; Shelby, R.A., et al. "Experimental Verification of a Negative Index of Refraction." *Science* 292 (April 6, 2001): 77–79.

22 THE BIOLOGY OF...PANIC

Gratacos, M., et al. "A Polymorphic Genomic Duplication on Human Chromosome 15 Is a Susceptibility Factor for Panic and Phobic Disorders." *Cell* 106 (August 10, 2001): 367.

Read more about the great naturalist's woes: Barloon, Thomas J., and Russell Noyes Jr. "Charles Darwin and Panic Disorder." *Journal of the American Medical Association* 277 (January 8, 1997): 138.

For more about psychiatric genetics, see Jonathan Flint's Web page: www.well.ox.ac.uk/flint; to learn about clinical aspects of anxiety disorders and Brad Schmidt's work, see anxiety.psy.ohio-state.edu; and for more on the evolutionary perspective from Randolph Nesse, see www-personal.umich.edu/~nesse/Articles/Fear&Fitness-Ethol&Sociobiol-1994.PDF.

24 VITAL SIGNS

For information on porphyria, see the Web site of the American Porphyria Foundation at www.enterprise.net/apf.

To read about the madness of King George III, see www.mhhe.com/biosci/ap/seeleyap/cardio/reading20.mhtml.

26 WORKS IN PROGRESS

Find out more about what mutant flies can teach us at the San Francisco Exploratorium Web site: www.exploratorium.edu/exhibits/mutant_flies/mutant_flies.html.

Read a brief history of the fly's service to science in *Fly: The Unsung Hero of 20th-Century Science* by Martin Brookes, HarperCollins, 2001.

29 SKY LIGHTS

NASA's "Basics of Space Flight" Web site contains a tutorial about the hows and whys of getting into space: www.jpl.nasa.gov/basics.

Learn about specific space-propulsion systems at the *Deep Space 1* site (nmp.jpl.nasa.gov/ds1) and the Planetary Society's solar sail project site (www.planetary.org/solarsail).

32 GUTH'S GRAND GUESS

Alan Guth's book, *The Inflationary Universe: The Quest for a New Theory of Cosmic Origins* (Perseus Books, 1997), is the definitive layperson's guide to his work.

For a complete guide to the Big Bang theory and related concepts, check out the Web site for NASA's Microwave Anisotropy Probe: map.gsfc.nasa.gov/m_uni.html.

40 DRIVING SIMULATOR

Find background information and see the National Advanced Driving Simulator in action at www-nrd.nhtsa.dot.gov/departments/nrd-12/NationalAdvancedDriverSimulator.html.

For more on the Iowa NADS facility, visit www.nads-sc.uiowa.edu.

The Department of Transportation's National Highway Traffic Safety Administration Web site is www.nhtsa.dot.gov.

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46 TALKING PLANTS

Read the book that started people talking to their plants: *The Secret Life of Plants* by Peter Tompkins and Christopher Bird. HarperCollins, 1989 (reprint of the 1974 Avon Books version).

David Attenborough's fascinating *The Private Life of Plants: A Natural History of Plant Behaviour* (Princeton University Press, 1995) covers all aspects of plant survival and is full of stunning photography. It's also available as a six-volume video set, produced by the BBC.

Biochemical Systematics and Ecology 29 (November 2001). Compiled by Marcel Dicke and Jan Bruin, this special issue is filled with scientific papers on chemical communication between plants.

52 BAD GENES, GOOD DRUGS

For an excellent primer on SNPs, see the Human Genome Project Information pages: www.ornl.gov/hgmis. Check out the SNP Fact Sheet at www.ornl.gov/hgmis/faq/snps.html.

See also the SNP Consortium home page at snp.cshl.org/about.

Learn about microarrays and genetic variation at the Perlegen site: www.perlegen.com.

Find out about ataxia-telangiectasia from the A-T Children's Project at www.atcp.org or the NIH at www.ncbi.nlm.nih.gov/cgi-bin/SCIENCE96/gene?ATM.

60 DO WE KILL WHALES WITH SOUND?

For more about cetacean hearing, read Darlene Ketten's chapter "Cetacean Ears" in Au, Whitlow W. L., et al. *Hearing by Whales and Dolphins.* New York: Springer, 2000.

A discussion of the adaptation of seals to their marine environment can be found at polarmet.mps.ohio-state.edu/ASPIRE_99/seals/science/evtxt.htm.

A good description of cochlear implants appears at www.wog.com/cochlear.html.

To read about Ketten and Margaret Skinner's insight into the placement of cochlear implants, see Ketten, Darlene, et al. "In Vivo Measures of Cochlear Length and Insertion Depth of Nucleus Cochlear Implant Electrode Arrays." *Annals of Otology, Rhinology, and Laryngology* 107 (November 1998): 1–16.

66 NOTES FROM A PARALLEL UNIVERSE

News and anecdotes about science cranks, plus links to cranks' Web sites and a crank o' the day: www.crank.net.

Read Eugene Sittampalam's "Theory of Everything" on his personal Web site: homepages.msn.com/Terminus/eugenes/01.Welcome.htm.

A short biography of Indian mathematician Srinivasa Ramanujan: www-groups.dcs.st-and.ac.uk/~history/Mathematicians/Ramanujan.html.

Information about Stanley Prusiner and his work: www.nobel.se/medicine/laureates/1997/index.html.

Sarah Simons, ed. *No One May Ever Have the Same Knowledge Again: Letters to Mount Wilson Observatory 1915–1935.* Los Angeles: Society for the Diffusion of Useful Information Press, 1993.

72 REVIEWS

For a brief history of J. Robert Oppenheimer's life, see www.labri.fr/Equipe/CombAlgo/membre/loeb/tree/julius.html. Read about the Manhattan Project at www.childrenofthemanhattanproject.org/index.htm.

Conservation International in Guatemala: www.conservation.org/xp/CIWEB/regions/meso_america/guatemala/guatemala.xml. Check out the beautiful and endangered quetzal at www.geocities.com/endangeredsp/SAmericaB28.html.

81 BOGGLERS

The original work on the squared rectangle problem was done by William Tutte, C.A.B. Smith, A. H. Stone, and R. L. Brooks in 1938, culminating in the discovery of a squared square (a square divided into squares of all different sizes). It has recently been proved that the smallest possible number of squares in a squared square is 21. For more about the *Mathematica* exhibition, see www.eamesoffice.com (Eames Office), www.exploratorium.edu (the Exploratorium in San Francisco), and www.mos.org (Boston Museum of Science).

88 NEUROQUEST

A list of books relating to vestibular sensation and its disorders can be found at www.geocities.com/otolithic/bookstore.htm.

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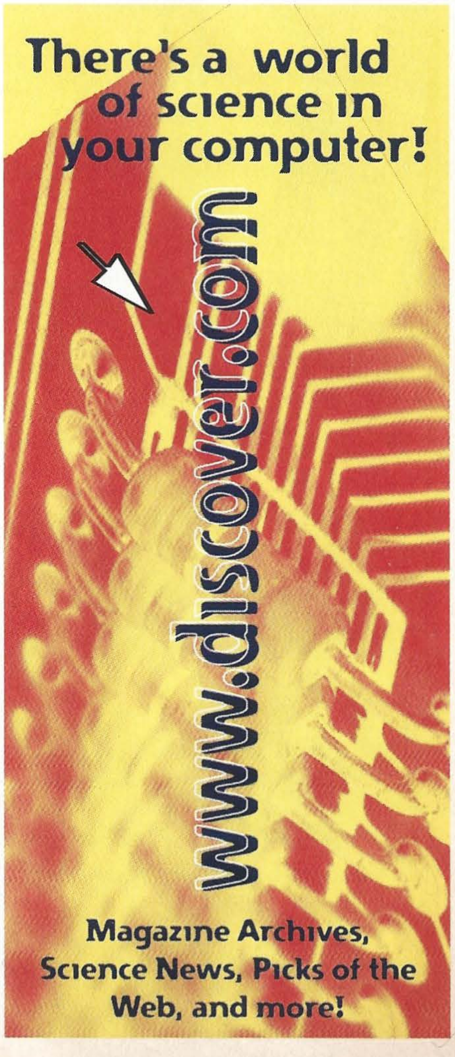
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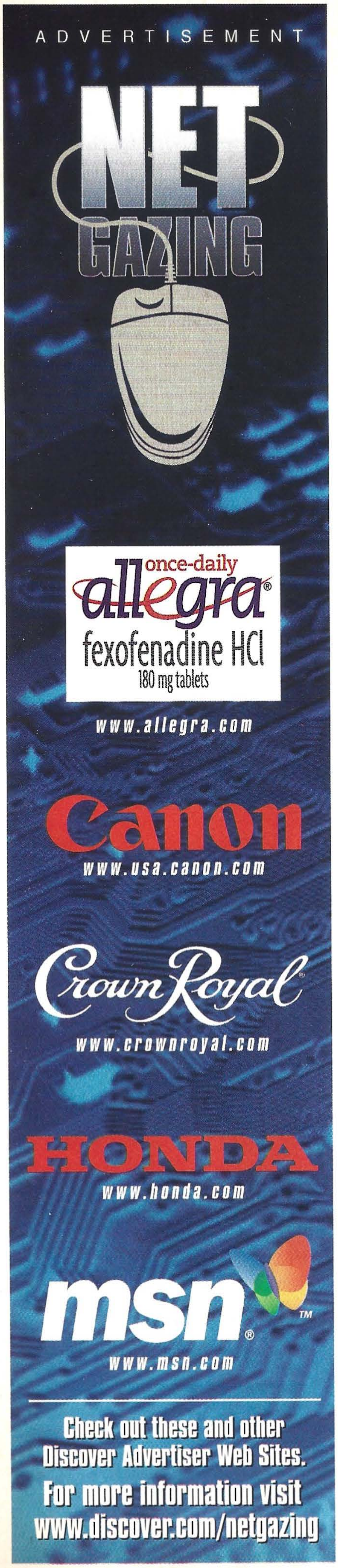

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(continued from page 8)

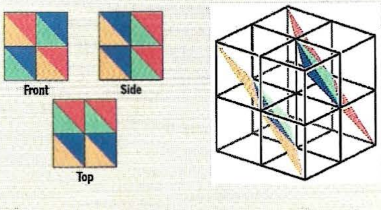
Eric Haseltine responds: *Dark matter may include both heavy and light ordinary elements bound up in brown dwarfs, white dwarfs, or clouds of gas. Supernovas still occur occasionally—about once a century in the Milky Way—spewing all kinds of detritus into space, including heavy elements. I'm not certain how much heavy-element "fog" these events might create, but I doubt that they would fill space chockfull because stars are typically pretty far apart from each other (separated by millions of star diameters), and most of them do not die in supernovas.*

Regarding question 4 (Do neutrinos have mass?): Some 13 years ago, the Kamiokande and Irvine Michigan Brookhaven neutrino detectors measured the time-of-flight difference between the arrival of light and the arrival of neutrinos from a new supernova. Some scientists announced that the potential error in measurement of this difference was small enough to preclude neutrinos having a mass of more

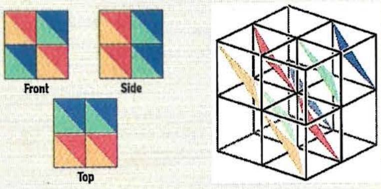
BOGGLERS SOLUTIONS

LOVE TRIANGLES

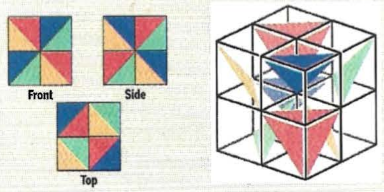
1. Two big parallel triangles in the cube.



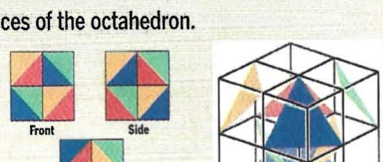
2. This configuration is the same as configuration 1, except that the red and blue triangles have been moved. There are now four planes of triangles in the cube. As in answer 1, all the triangles are parallel.



3. Four of the triangles touch each other at the center, and another four touch in a ring around the center.

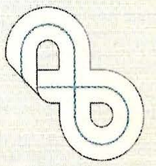


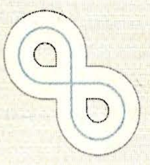
4. This configuration is the same as configuration 3, except that each triangle has been turned upside down. Four triangles on the inside form every other face of an octahedron around the center. Four others hover outside the missing faces of the octahedron.



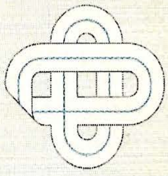
MÖBIUS STRIP

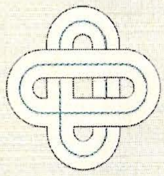
1. Surprisingly, a cut down the middle gives you a single loop of paper instead of two. The loop now has three twists.
2. You need two trains. The two parallel tracks traverse "both" sides of the Möbius strip, then return to their original points.
3. You end up with two loops. The middle third remains an ordinary Möbius strip, and the outer two-thirds of the loop forms a second, double-length loop linked to the first loop.
4. One train: Two trains (or glue the ends to make two Möbius strips):



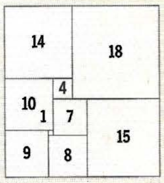


Three trains: Four trains:

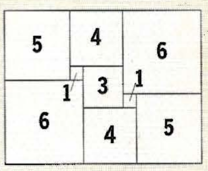




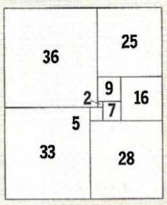
SQUARE DANCE



Ex.



1.



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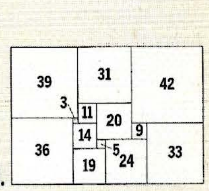

3.

For more information about these problems, please turn to our Resources section on page 82.

than 10 electron volts. I understood this to mean that oscillating neutrinos would not be possible. That would present a big problem for cosmologists, since they need oscillating neutrinos to explain the electron-neutrino shortage from the sun. Later pronouncements said that neutrinos do have mass, enough to permit oscillations. Has anyone reconciled the differences between the two announcements?

C. NORMAN WINNINGSTAD—Newport, Oregon

Eric Haseltine responds: *As you suggest, supernovas are extremely useful in studying neutrino masses because these cataclysmic events emit copious amounts of both light and neutrinos. If neutrinos are massive, then they will travel more slowly than photons of light, which are massless. So any observed time-of-flight differences between neutrinos and photons from a single supernova strongly suggest that neutrinos do indeed possess mass. Data from the 1987 supernova you mentioned place an upper limit on this mass at 30 electron volts (mass and energy are equivalent according to* $E=mc^2$*, so very small masses are often conveniently described as energy in terms of electron volts). There is no theoretical reason why this value—or even values much lower than 30 electron volts—should preclude neutrino oscillations (neutrinos changing from one type to another, such as a mu neutrino to an electron neutrino). A survey of the literature reveals a number of plausible models in which neutrinos oscillate with masses smaller than .1 electron volt. The bottom line is that there is no contradiction between the supernova data and more recent data on neutrino oscillation coming from the Super-K neutrino detector in Japan.*

"The 11 Greatest Unanswered Questions of Physics" boggles my mind and takes it to a philosophical conundrum. Since we don't expect our cousins the chimpanzees ever to comprehend calculus, doesn't it follow that there may be a super-set of knowledge that lies beyond the comprehension of mere human minds? A point of near-infinite energy expanding much faster than the speed of light with random quantum fluctuations in density makes me wonder: Just how would one chimp explain a differential equation to another?

RUSS AGREEN—Denton, Maryland

ERRATUM

The article "Photography, Old & New Again" [February] was fascinating, but I must correct the caption of the insect pictured on page 51. The insect is identified as a New Guinea beetle, but it is actually an adult female of the stick insect *Heteropteryx dilatata,* which as I recall is native to Malaysia.

CARL MOXEY, PH.D., SENIOR LECTURER, BIOLOGY
Northeastern University, Boston, Massachusetts

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THE SIXTH SENSE

Automatic protection from gravity

BY ERIC HASELTINE

YOU MAY NOT REALIZE IT, BUT YOU ARE ENDOWED WITH A form of extrasensory perception that makes it possible to detect things you cannot hear, feel, smell, taste, or touch. The extraordinary gift is called vestibular sensation.

This sixth sense, which monitors the direction and velocity of your head movements, derives its name from vestibules (literally, little entry halls) in the inner ears. The chambers are populated with tiny hairs that bend with moving fluid whenever your head shifts position. Sensors get excited when follicles are displaced, and the excitations lead to perceptions of head movement that in turn make it possible for you to maintain balance.

One reason vestibular organs get no respect is that unlike eyes, ears, noses, tongues, and skin, they're invisible to us. Another reason is that the sensations they produce don't typically rise to the level of consciousness. Finally, the brain exploits vestibular signals in ways that are often counterintuitive.

You can catch this stealthy sixth sense at work by flirting with the force of gravity in the following experiments.

EXPERIMENT 1 With your feet close together and your body upright, allow yourself to fall forward. As you reach the tipping point, first one leg and then both your arms will jut out in front of you. These involuntary limb movements are part of the vestibulospinal reflex that is triggered when your inner ear senses that your head is moving out of its stability zone (the region surrounding your vertical axis, within which you can move without falling over). The vestibular organs command nerve cells in your spinal cord to contract the leg and shoulder muscles that cause your leg and arms to extend.

At first blush, these arm movements make no sense because they shift your center of gravity forward, leaving you even more likely to tip over. But the arm reflexes position your hands to cushion a potential fall. Your brain unconsciously believes—based on millions of years of evolutionary experience of *Homo sapiens* and our various ancestors—that preparing to absorb the shock of a fall (by pushing your arms out) is more likely to prevent bodily harm than attempting to prevent the spill in the first place (by moving your arms and center of gravity backward).

EXPERIMENT 2 Your inner ears work closely with your eyes. To find out just how closely, place your right heel directly in front of your left toe, as if standing on a balance beam. Then, after 15 seconds, close your eyes.

Unless you have truly exceptional poise—that of a gymnast, for example—you'll start to wobble, because vision provides important reference cues about your position that help the brain keep you upright. However, one of the baffling things about the vestibular system is that it does not always work harmoniously with the visual system.

To demonstrate this, stand up and quickly spin around, completing five revolutions. Then close your eyes and come to an abrupt stop. You'll feel woozy for at least a few seconds because the fluid in your inner ear, like sloshing water in a drinking glass, doesn't immediately stop when you do. The motion of the fluid tells the brain that you are moving.

Now repeat the procedure, this time keeping your eyes open the whole time. Odds are the feeling of nausea you experience will be worse when you come to a sudden stop because the added visual cues (which report that you are stationary) create sensory warfare in your brain.

Incidentally, if you ever find yourself feeling dizzy without having abused yourself like this, get a checkup, because your inner ear is sensitive to a wide range of medical conditions, such as infections, that merit treatment. ☒

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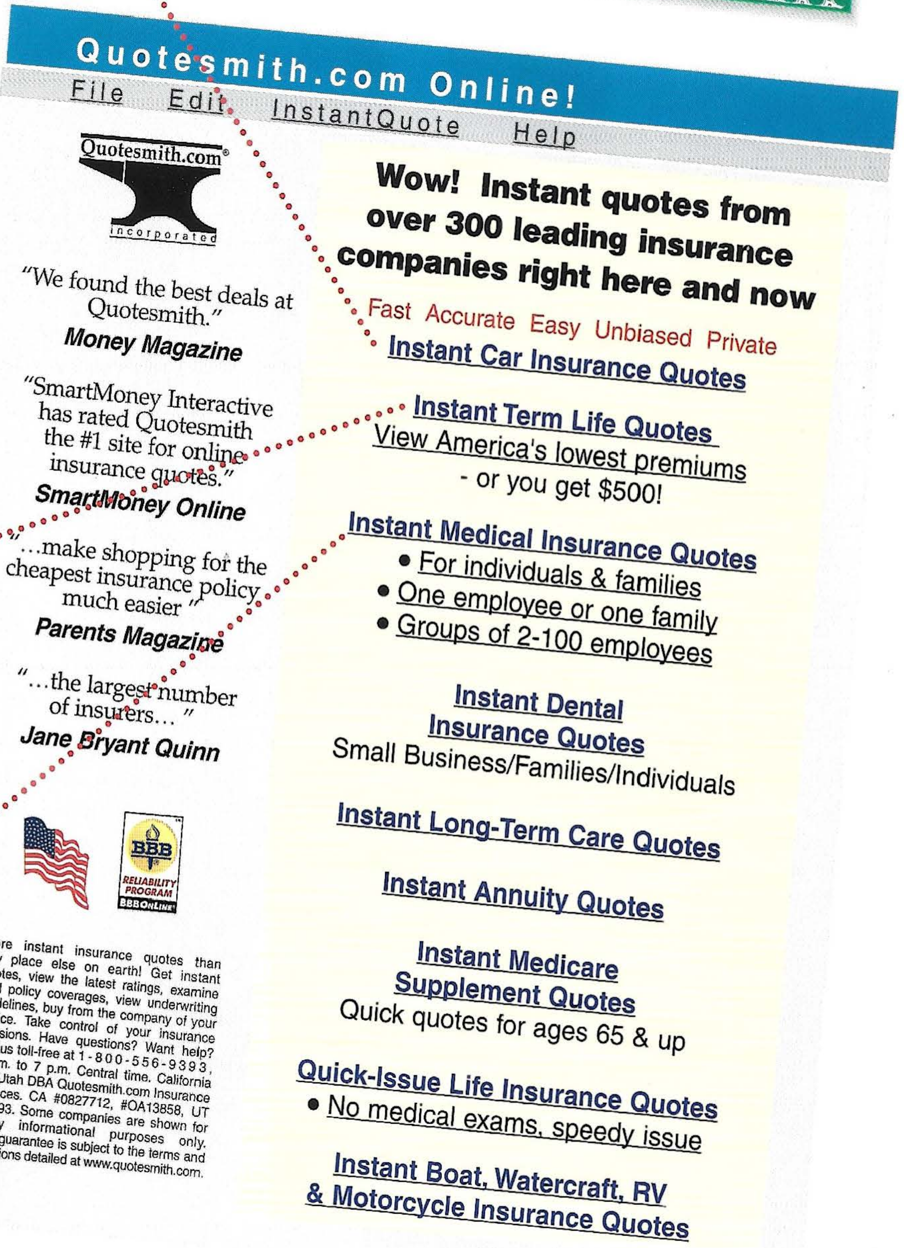

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